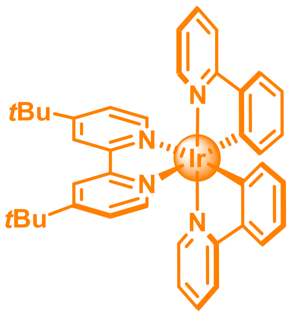
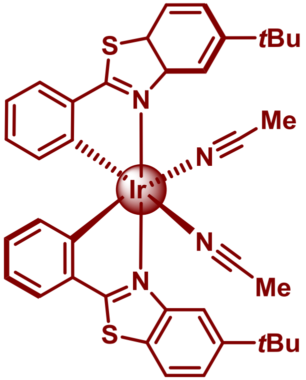
Visible Light Photoredox Catalysis with Transition Metal Complex.
Merging Photoredox and Asymmetric Catalysis





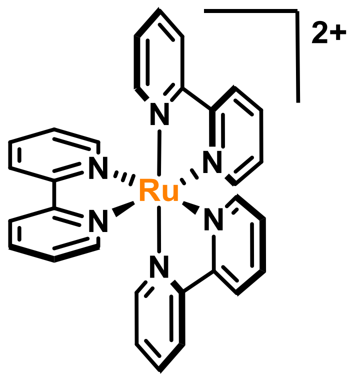
Literature Seminar 2016.05.21
Benjamin Ovadia

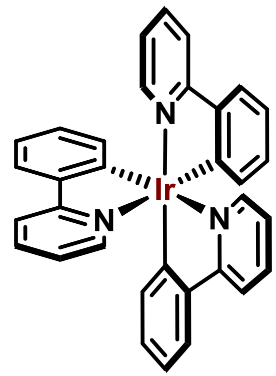
Mechanism of Action of Photoredox Catalysts

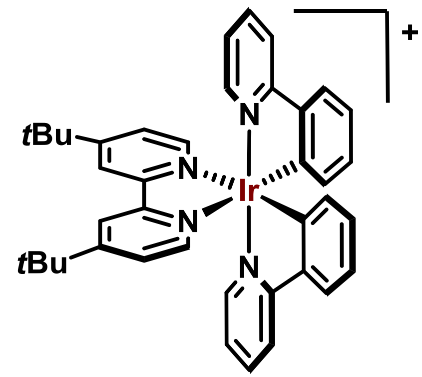
Application of Photoredox Catalysis in Organic Synthesis

Cooperative Photoredox Catalysis and Asymetric Catalysis

Common Transition Metal Photocatalysts





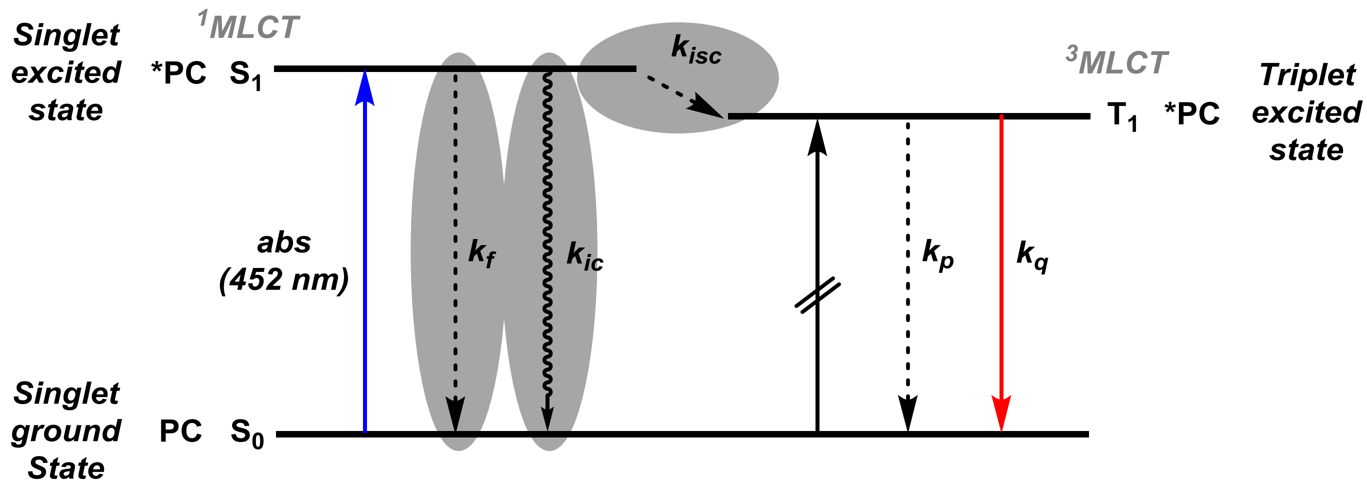


	$Ru(bpy)_3Cl_2$	**$Ir(ppy)_3$**	**$Ir(ppy)_2(dtbbpy)PF_6$**
Reduction potentiel	$E(Ru^{3+}/{}^*Ru^{2+})$= -0.81 V	$E(Ir^{4+}/{}^*Ir^{3+})$= -1.73 V	$E(Ir^{4+}/{}^*Ir^{3+})$= -0.96 V
Oxidation potentiel	$E({}^*Ru^{2+}/Ru^{+})$= +0.77 V	$E({}^*Ir^{3+}/Ir^{2+})$= +0.31 V	$E({}^*Ir^{3+}/Ir^{2+})$= +0.66 V
Excited state lifetime	τ= 1.1 μs	τ= 1.9 μs	τ= 0.56 μs
Max. wavelength of excitation	λ_{abs}= 452 nm	λ_{abs}= 375 nm	λ_{abs}= 410 nm
Max. wavelength of emission	λ_{em}= 652 nm	λ_{em}= 494 nm	λ_{em}= 581 nm

Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322.
Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 1617.

Photoelectronic Properties of Photocatalysts

Formation of the photocatalyst excited state: Jablonski diagram



MLCT: Metal to Ligand Charge Transfer

S_1 relaxations

K_{isc}= intersystem crossing to T_1 — *Rapid conversion from singlet (τ= 300 fs) to long lived triplet excited state (τ= 1100 ns)*

K_f= fluorescence (452 nm) — *Fast emission of photon, same λ as the one it absorbed*

K_{ic}= internal convertion — *Non-radiative de-excitation through bond vibration. Heat loss*

Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322.
Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 1617.

Photoelectronic Properties of Photocatalysts

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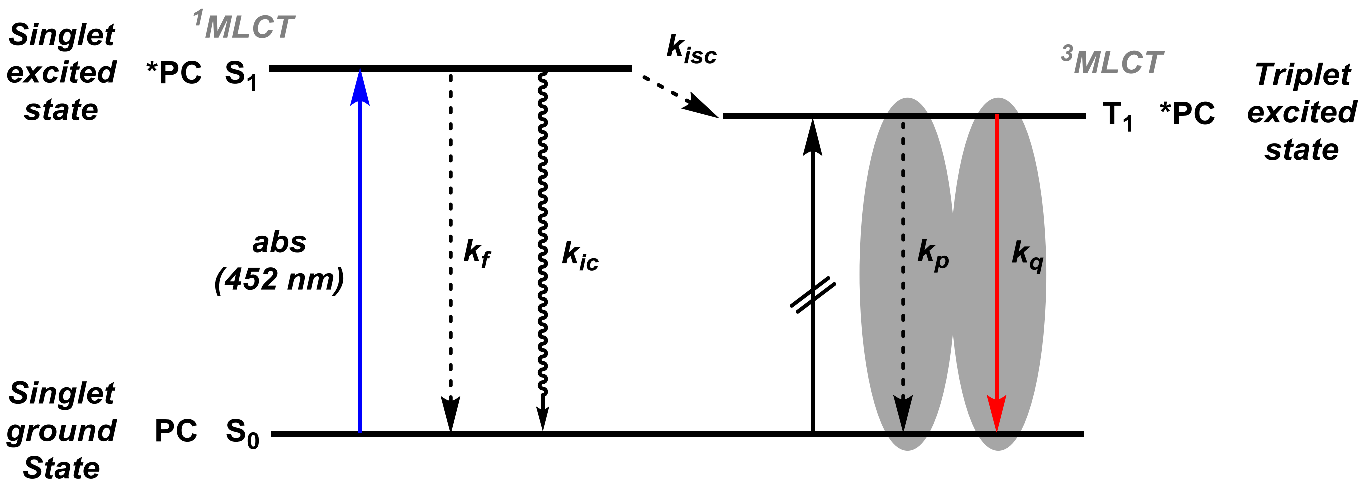


T_1 relaxations

Slow emission of photon — **K_p= phosphorescence (615 nm)**

Relaxation through electron transfer to another molecule — **K_q= intermolecular quenching**

Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322.
Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 1617.

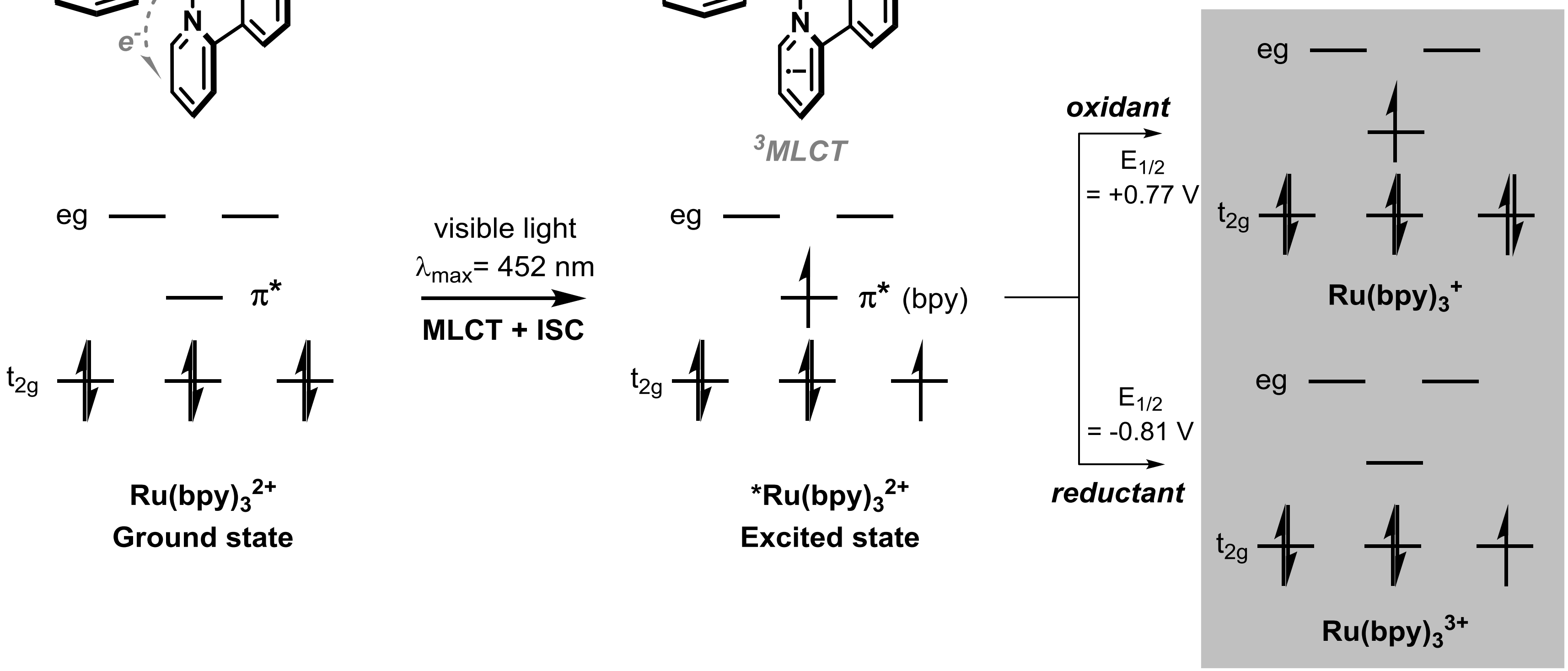
Photoelectronic Properties of Photocatalysts

Photochemistry of $Ru(bpy)_3^{2+}$: Molecular orbital depiction

Octaehedral, [Kr]5s^2 4d^6

$E_{1/2}^{III/*II}$= -0.87 V *vs.* $E_{1/2}^{III/II}$= +1.29 V

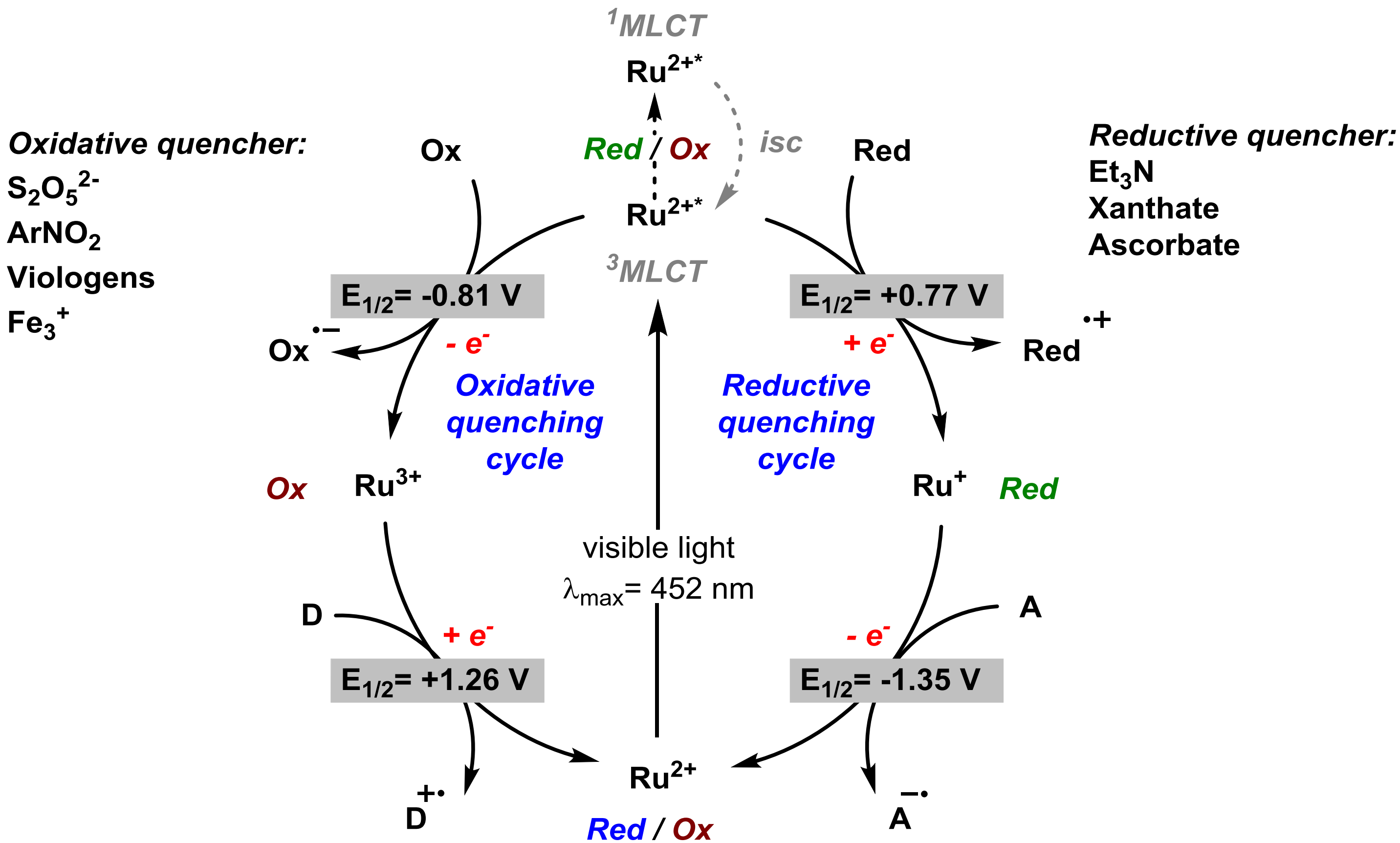
$E_{1/2}^{*II/I}$= +0.77 V *vs.* $E_{1/2}^{II/I}$= -1.33 V



Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322.
Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 1617.

Photoelectronic Properties of Photocatalysts

Mechanism of action of photoredox catalysts



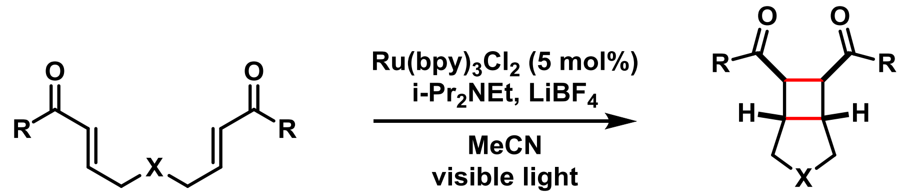
Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322.
Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 1617.

Mechanism of Action of Photoredox Catalysts

Application of Photoredox Catalysis in Organic Synthesis

Cooperative Photoredox Catalysis and Asymetric Catalysis

[2+2] Photocycloadditions of enones

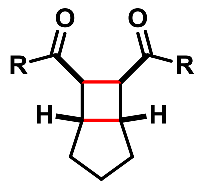


15 examples
up to 96% yield, d.r. 10:1

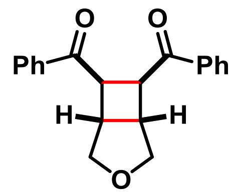
T.P. Yoon

Selected examples:

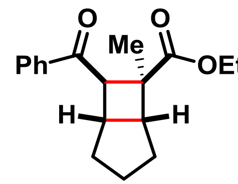
intramolecular [2+2] cycloaddition



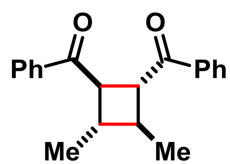
R= Ph, 89% yield, d.r. >10:1
R= 4-MeOPh, 98% yield, d.r. 10:1
R= 4-ClPh, 96% yield, d.r. 10:1
R= Me, 0% yield



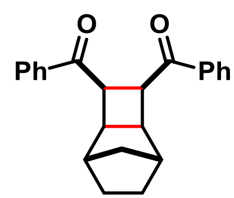
90% yield, d.r. 5:1



84% yield, d.r. 10:1

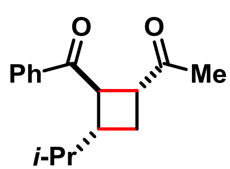


82% yield, d.r. >10:1

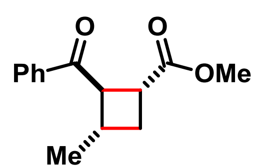


54% yield, d.r. 6:1

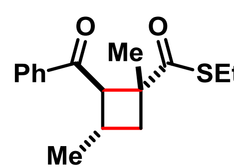
Crossed intermolecular [2+2] cycloaddition



64% yield, d.r. >10:1



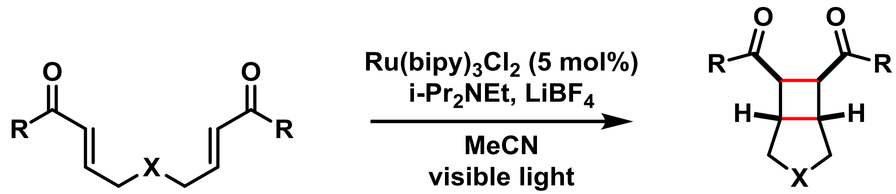
65% yield, d.r. 8:1



57% yield, d.r. 5:1

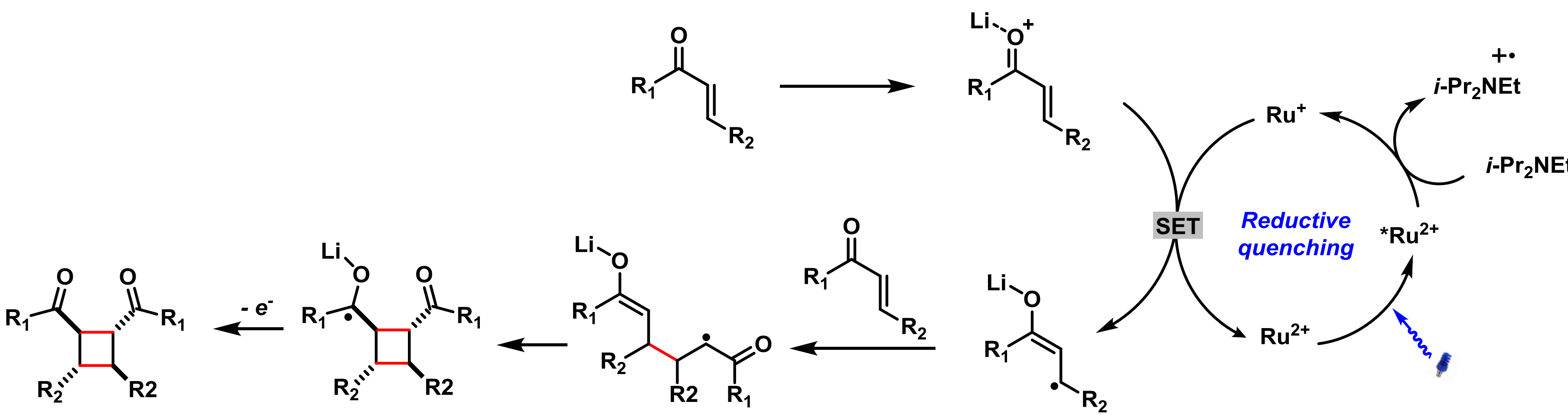
[2+2] Photocycloadditions of enones

T.P. Yoon



15 examples
up to 96% yield, d.r. 10:1

Proposed mechanism:

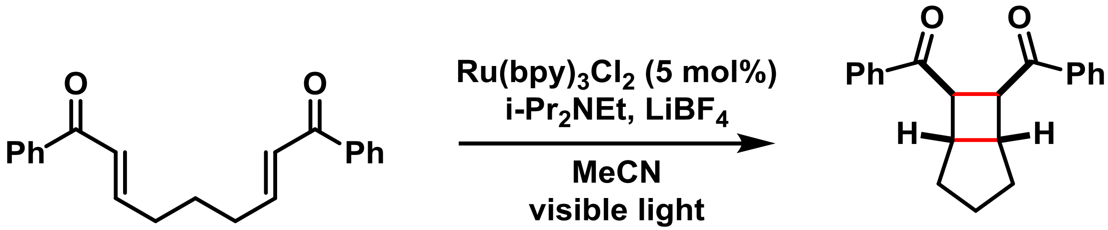


Ischay, M. A.; Anzovino, M. E.; Du, J.; Yoon, T. P. *J. Am. Chem. Soc.* **2008**, *130*, 12886.
Du, J.; Yoon, T. P. *J. Am. Chem. Soc.* **2009**, *131*, 14604.

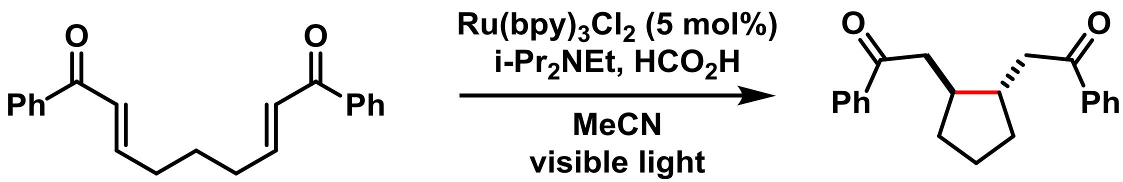
Reductive Photocyclization of enones

T.P. Yoon

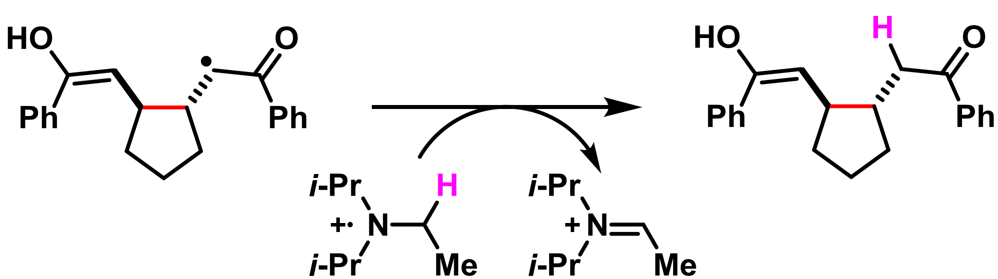
Lewis acid activation: **[2+2] cycloaddition**



Brönsted acid activation: **reductive coupling**



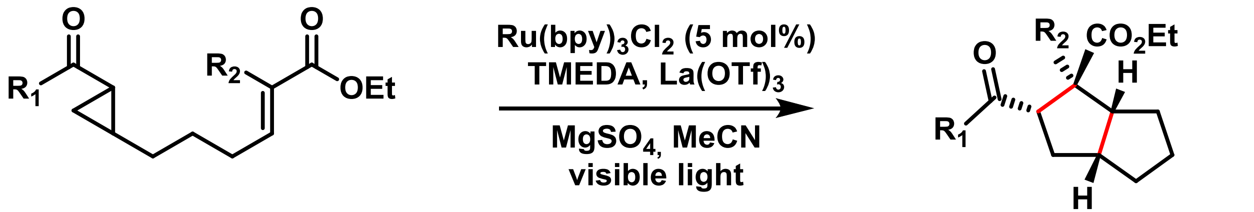
82% yield, d.r. >10:1



Du, J.; Espelt, L. R.; Guzei, I. A.; Yoon, T. P. *Chem. Sci.* **2011**, *2*, 2115.

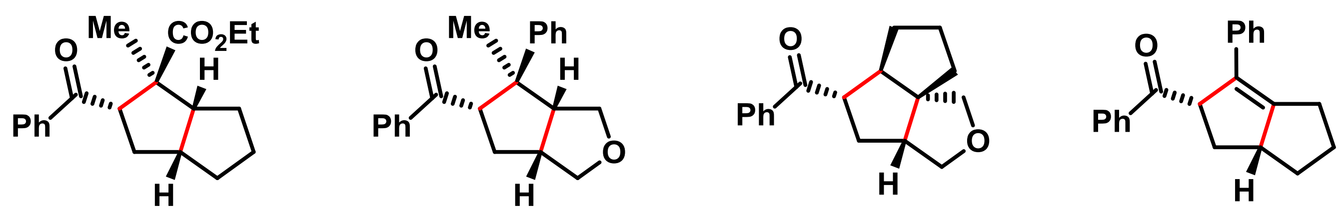
[3+2] Photocycloaddition of Aryl Cyclopropyl Ketones

WISCONSIN
UNIVERSITY OF WISCONSIN–MADISON



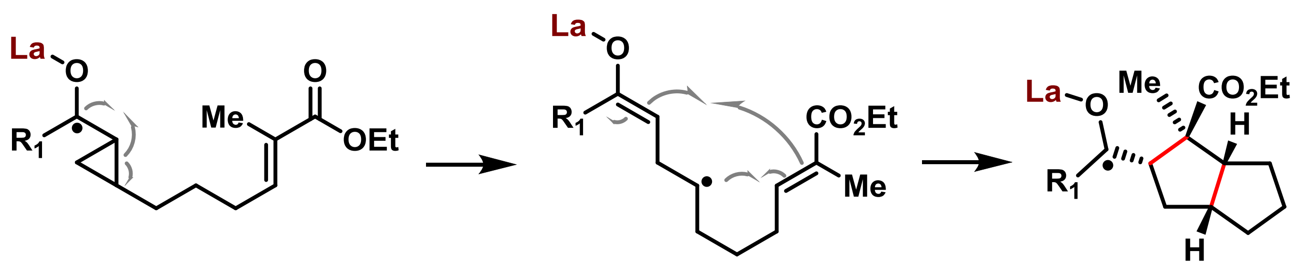
16 examples
55-83% yield, d.r. >10:1

Selected examples:



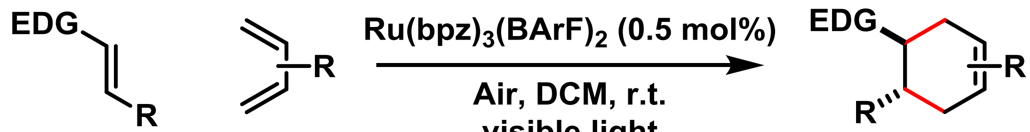
83% yield, d.r. 6:1 | 63% yield, d.r. 10:1 | 69% yield, d.r. 2:1 | 83% yield, d.r. 9:1

Proposed mechanism



Lu, Z.; Shen, M.; Yoon, T. P. *J. Am. Chem. Soc.* **2011**, *133*, 1162.

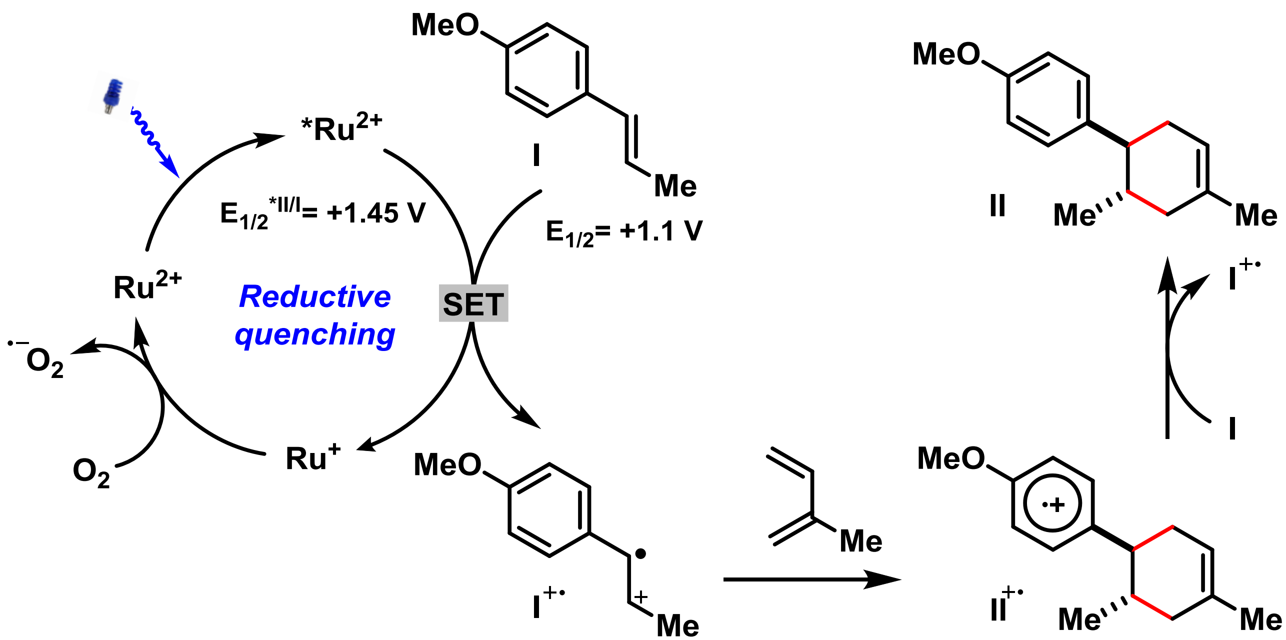
Radical Cation Diels-Alder PhotoCycloaddition



18 examples
up to 98% yield, d.r. 10:1

T.P. Yoon

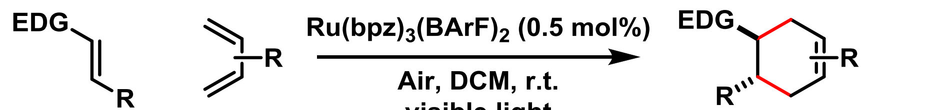
Proposed mechanism:



Lin, S.; Ischay, M. A.; Fry, C. G.; Yoon, T. P. *J. Am. Chem. Soc.* **2011**, *133*, 19350.

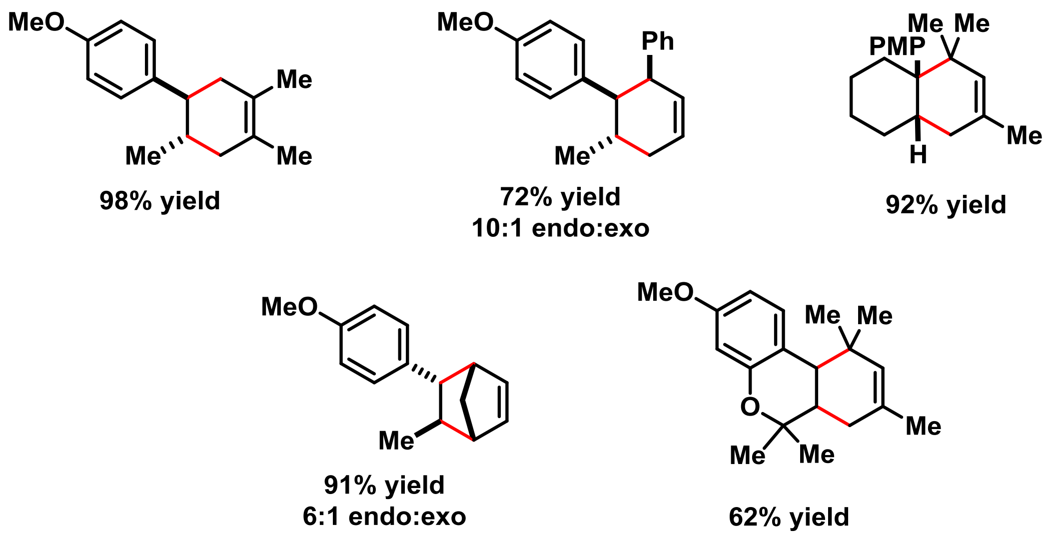
Radical Cation Diels-Alder PhotoCycloaddition

T.P. Yoon

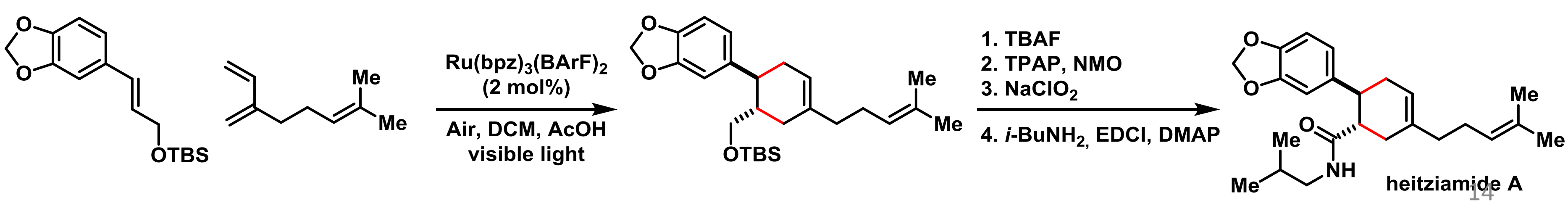


18 examples
up to 98% yield, d.r. 10:1

Selected examples:

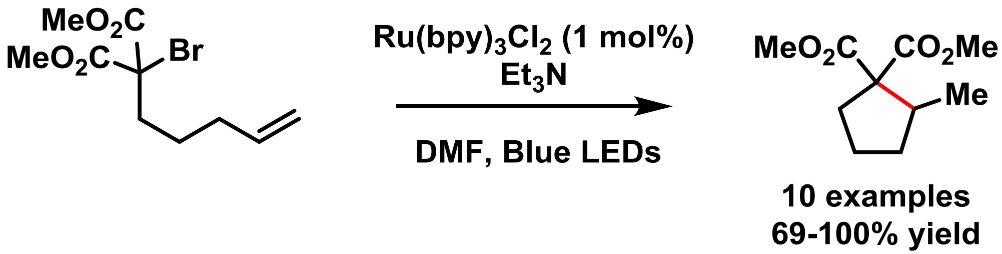


Total synthesis of heitziamide A:



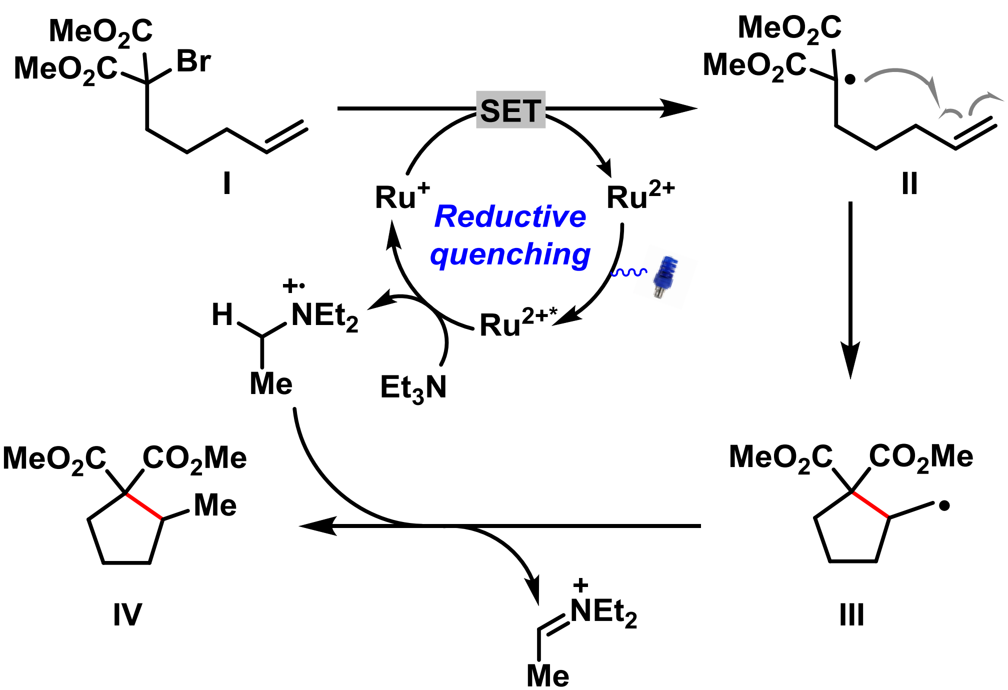
Lin, S.; Ischay, M. A.; Fry, C. G.; Yoon, T. P. *J. Am. Chem. Soc.* **2011**, *133*, 19350.

Reductive Radical Cyclization



C.R.J. Stephenson

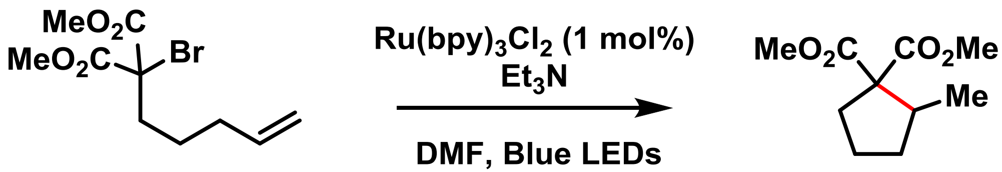
Proposed mechanism:



Tucker, J. W.; Nguyen, J. D.; Narayanam, J. M. R.; Krabbe, S. W.; Stephenson, C. R. J. *Chem. Commun.* **2010**, *46*, 4985.

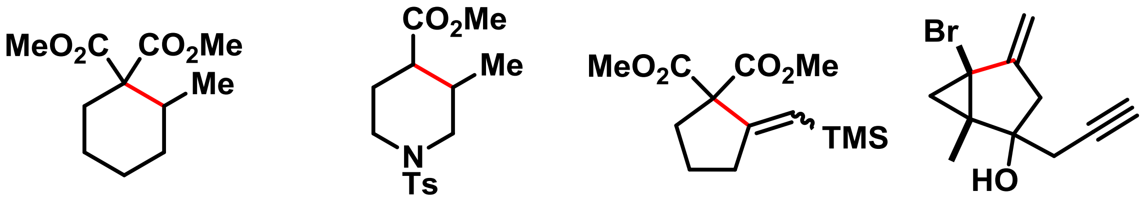
Reductive Radical Cyclization

C.R.J. Stephenson



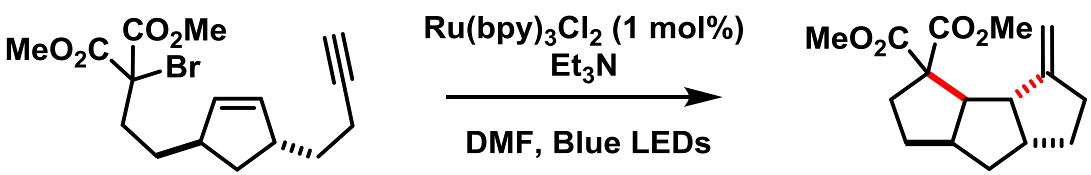
10 examples
69-100% yield

Selected examples:



69% yield | 84% yield (Ir catalyst) | 100% yield | 85% yield

Radical cascade cyclization:

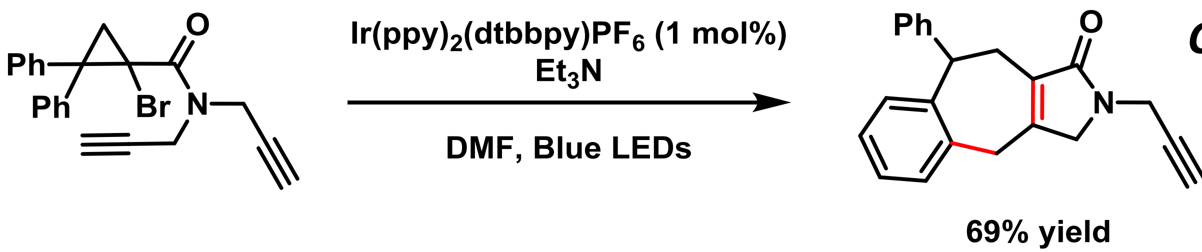


89% yield

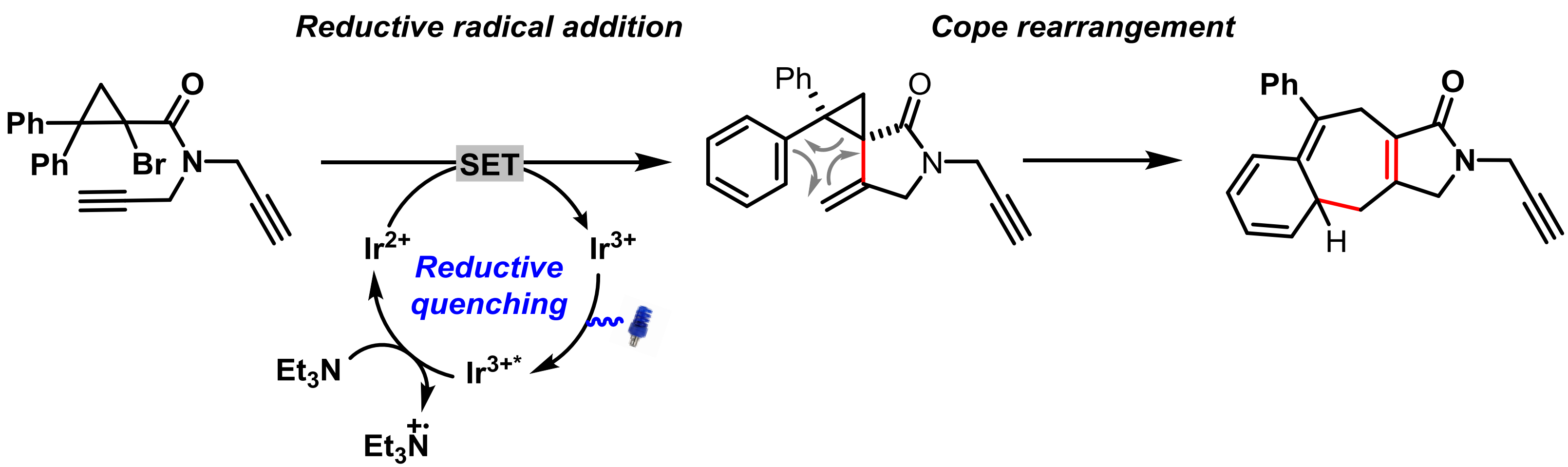
Tucker, J. W.; Nguyen, J. D.; Narayanam, J. M. R.; Krabbe, S. W.; Stephenson, C. R. J. *Chem. Commun.* **2010**, *46*, 4985.

Visible light-Mediated Cascade
Radical Cyclization/Cope Rearrangement

C.R.J. Stephenson



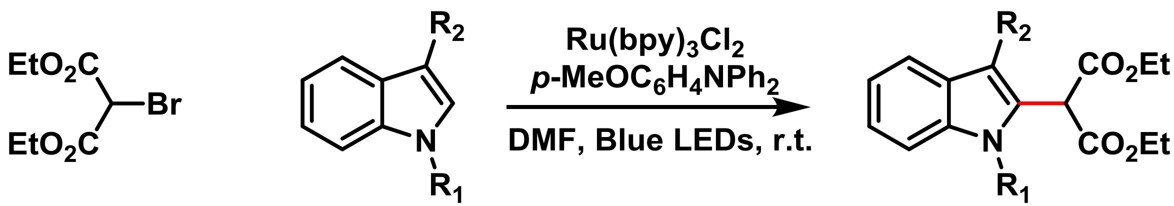
Proposed mechanism:



Tucker, J. W.; Stephenson, C. R. J. *Org. Lett.* **2011**, *13*, 5468.

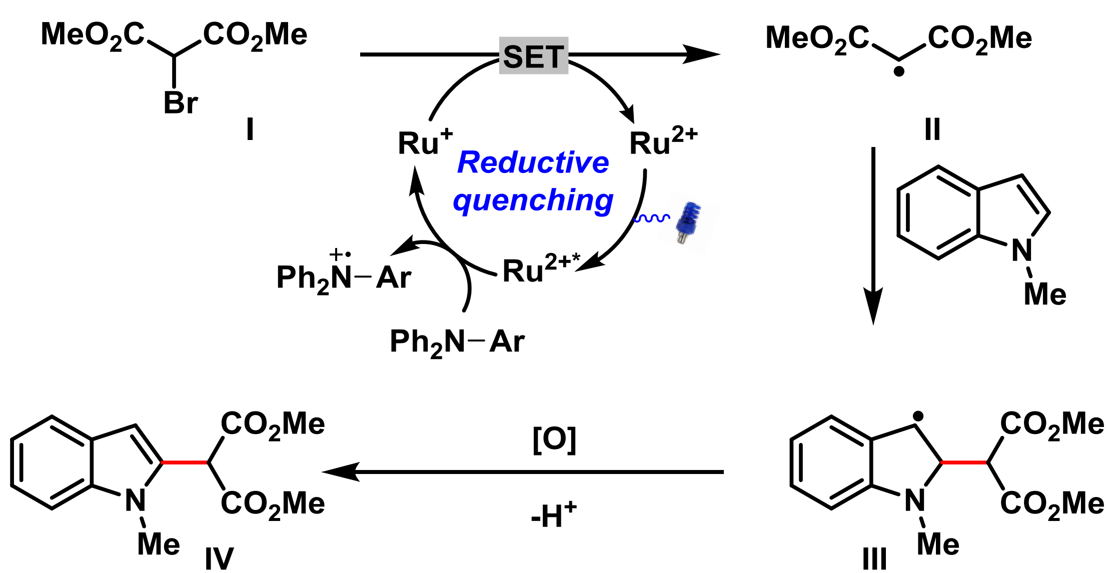
Visible light-Mediated C-H Functionalization of Heterocycles

C.R.J. Stephenson



14 examples
40 - 92 % yield

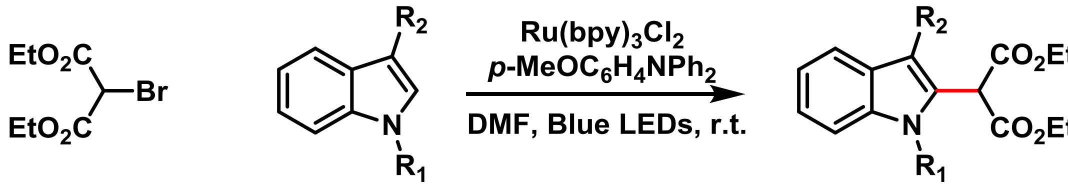
Proposed mechanism:



Furst, L.; Matsuura, B. S.; Narayanam, J. M. R.; Tucker, J. W.; Stephenson, C. R. J. *Org. Lett.* **2010**, *12*, 3104.
Tucker, J. W.; Narayanam, J. M. R.; Krabbe, S. W.; Stephenson, C. R. J. *Org. Lett.* **2010**, *12*, 368.

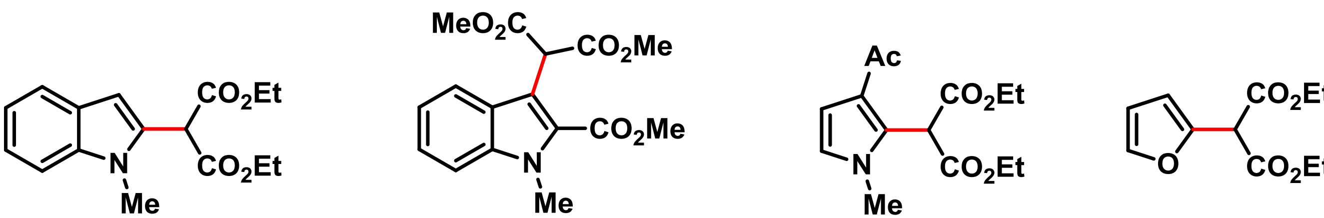
Visible light-Mediated C-H Functionalization of Heterocycles

C.R.J. Stephenson

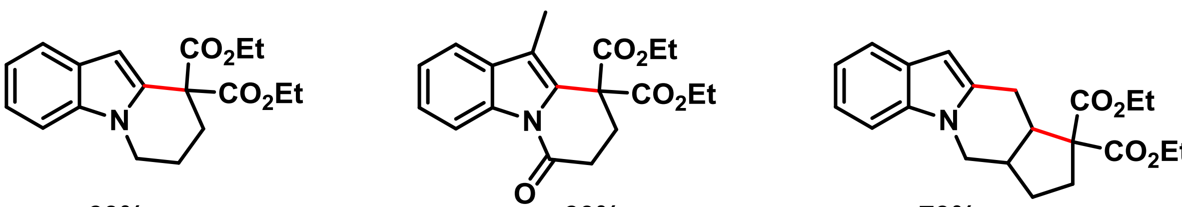


14 examples
40 - 92 % yield

Selected examples:



82% 92% 72% 68%



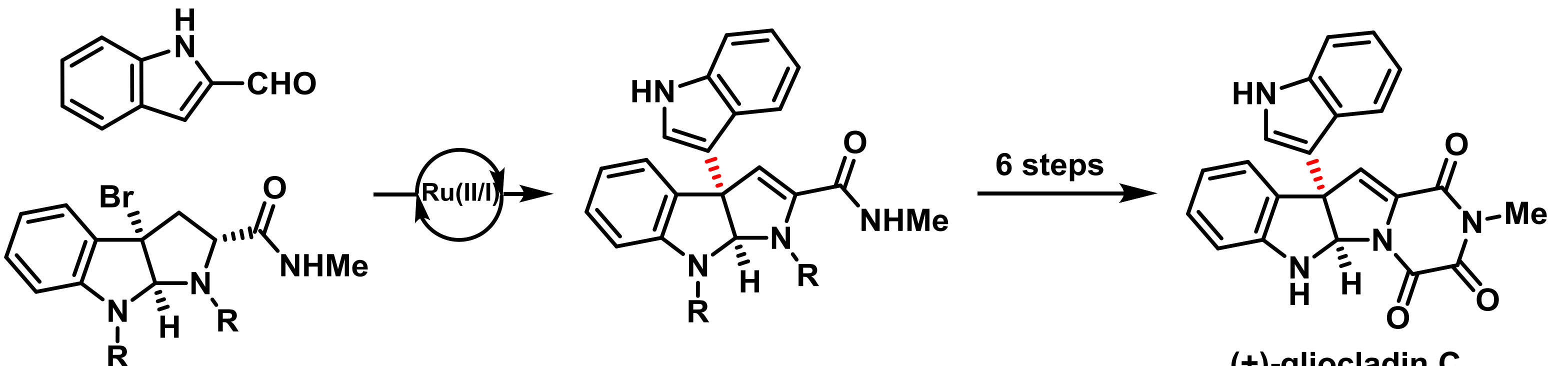
60% 60% 79%

Furst, L.; Matsuura, B. S.; Narayanam, J. M. R.; Tucker, J. W.; Stephenson, C. R. J. *Org. Lett.* **2010**, *12*, 3104.
Tucker, J. W.; Narayanam, J. M. R.; Krabbe, S. W.; Stephenson, C. R. J. *Org. Lett.* **2010**, *12*, 368.

Visible light-Mediated
C-H Functionalization of Heterocycles

C.R.J. Stephenson

Synthetic study of (+)-gliocladine C



(+)-gliocladin C

Furst, L.; Narayanam, J. M. R.; Stephenson, C. R. J. *Angew. Chem. Int. Ed.* **2011**, 50, 9655.

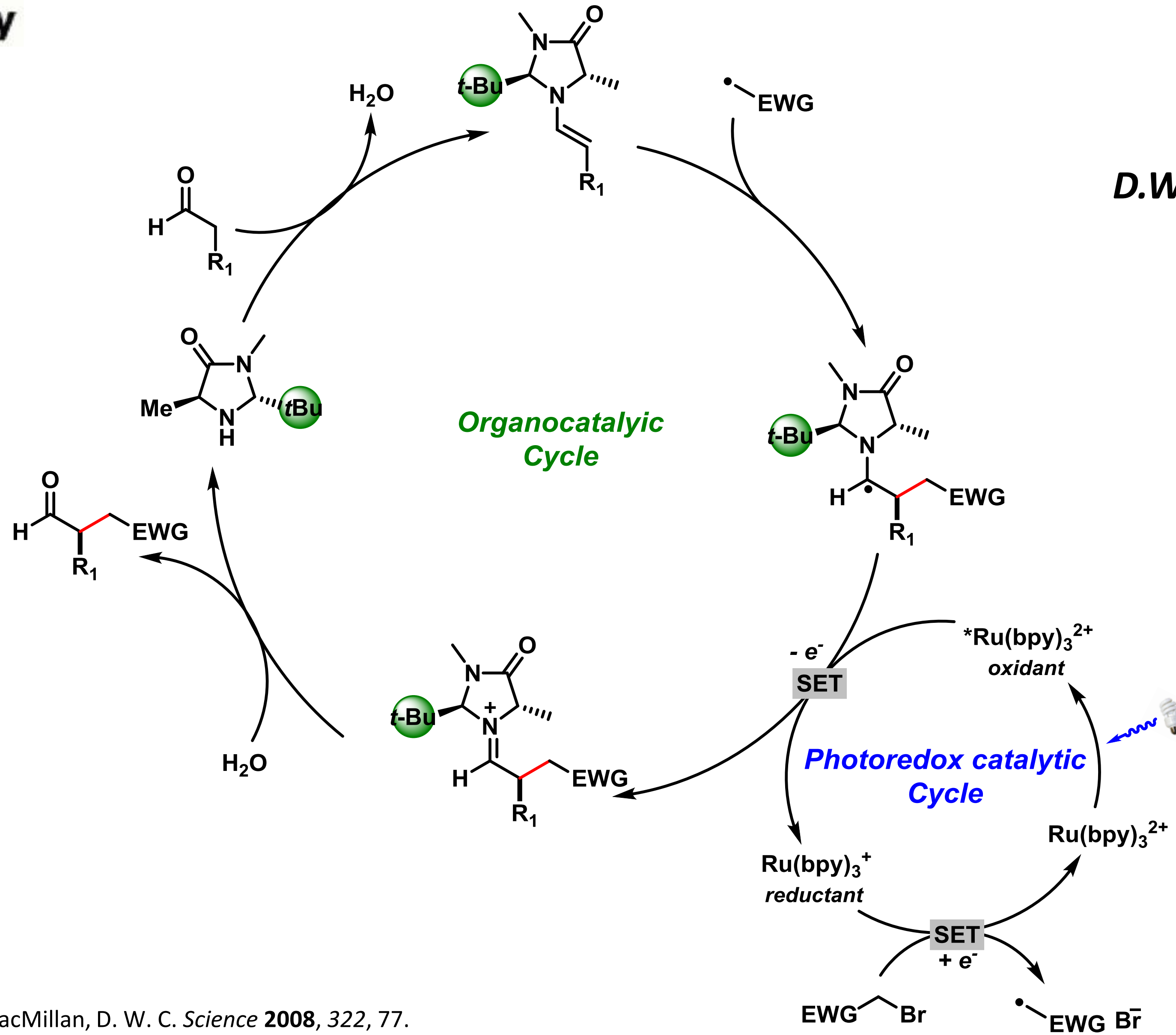
Mechanism of Action of Photoredox Catalysts

Application of Photoredox Catalysis in Organic Synthesis

Cooperative Photoredox Catalysis and Asymetric Catalysis

Enantioselective Alkylation of Aldehyde Merging Organocatalysis and Photoredox Catalysis

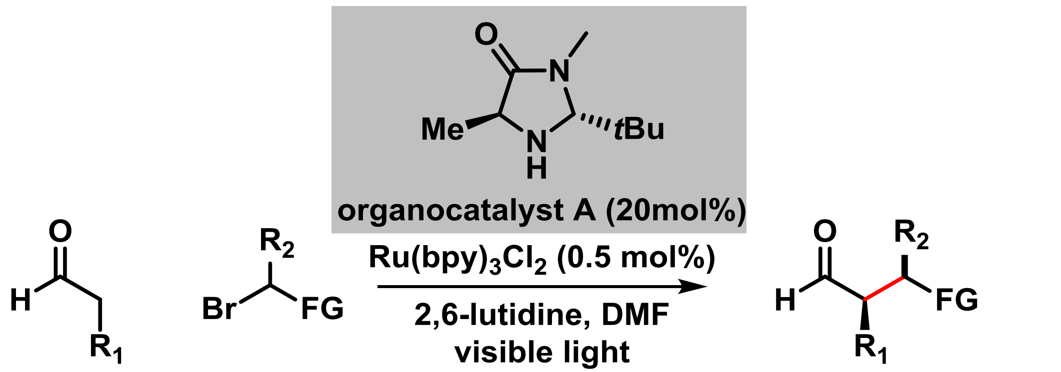
D.W.C. MacMillan



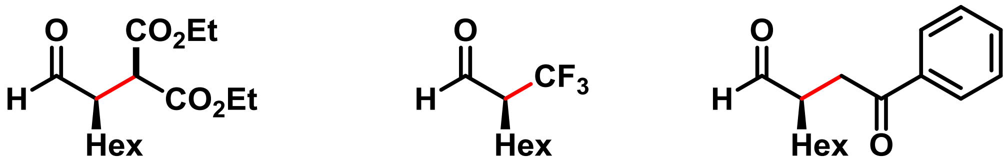
Nicewicz, D. A.; MacMillan, D. W. C. *Science* **2008**, *322*, 77.
Shih, H.-W.; Vander Wal, M. N.; Grange, R. L.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2010**, *132*, 13600

Enantioselective Alkylation of Aldehyde Merging Organocatalysis and Photoredox Catalysis

D.W.C. MacMillan



up to 93% yield, 99% ee

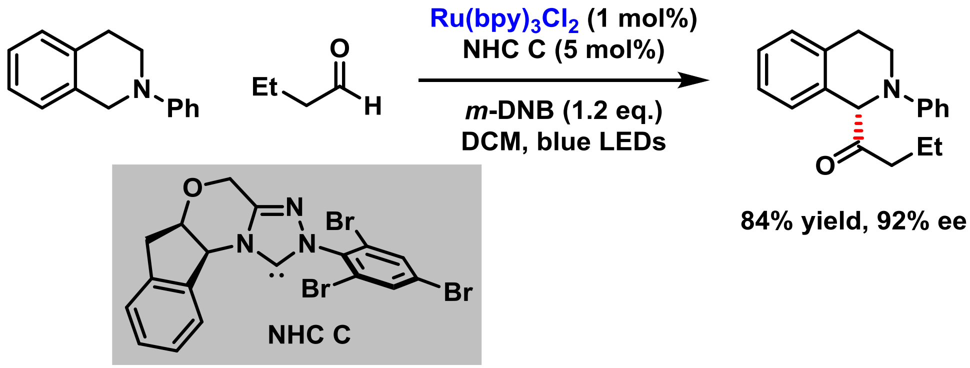


93% yield, 90% ee | 79% yield, 99% ee | 84% yield, 96% ee

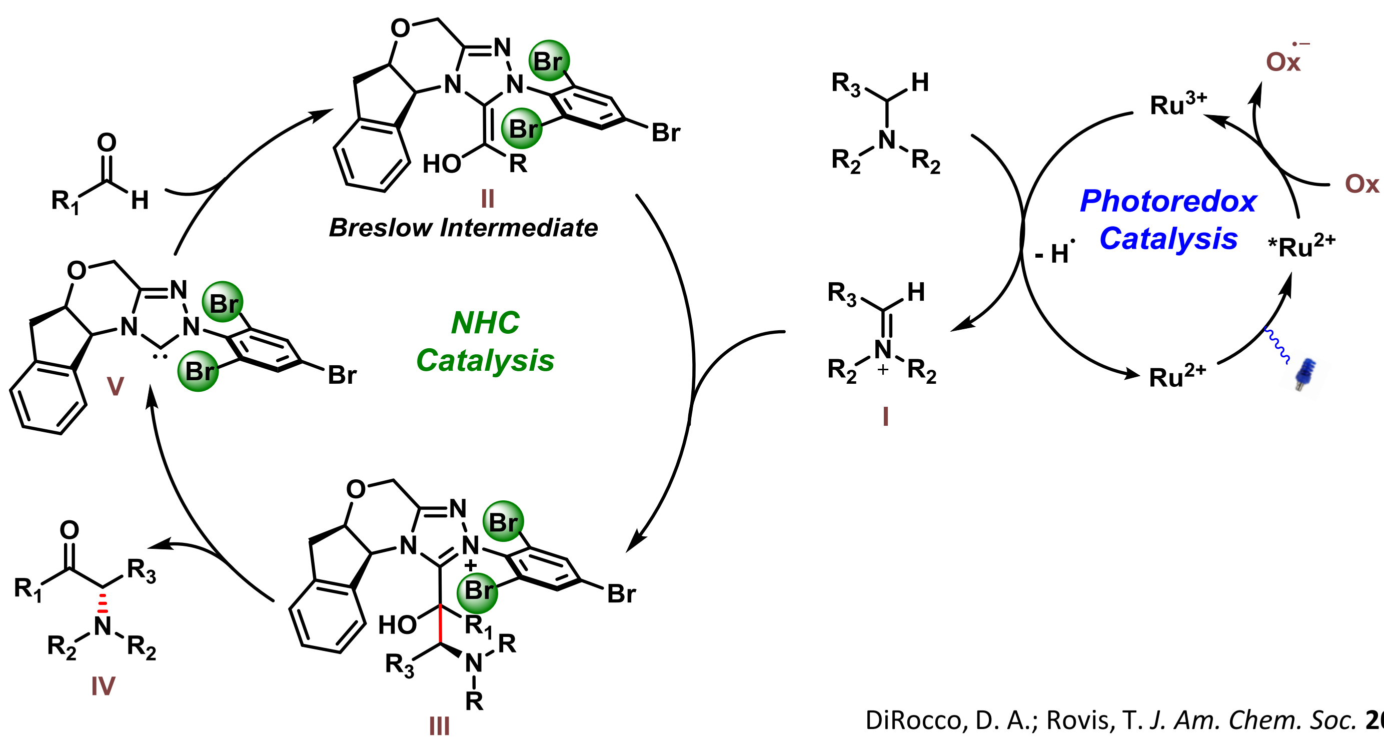
Nicewicz, D. A.; MacMillan, D. W. C. *Science* **2008**, *322*, 77.
Shih, H.-W.; Vander Wal, M. N.; Grange, R. L.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2010**, *132*, 13600

Enantioselective α-Acylation of Tertiary Amines. Photoredox Activation and NHC Catalysis

T. Rovis



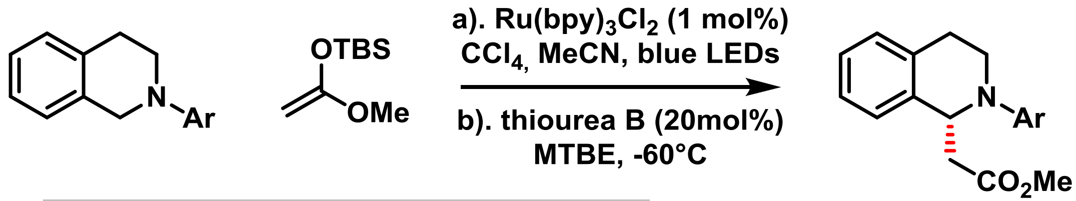
Proposed catalytic cycles:



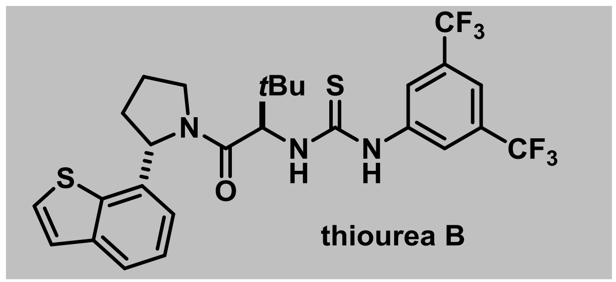
DiRocco, D. A.; Rovis, T. *J. Am. Chem. Soc.* **2012**, *134*, 8094.

Enantioselective Synthesis of β-Amino Esters. Photoredox Activation and Anion Binding Catalysis

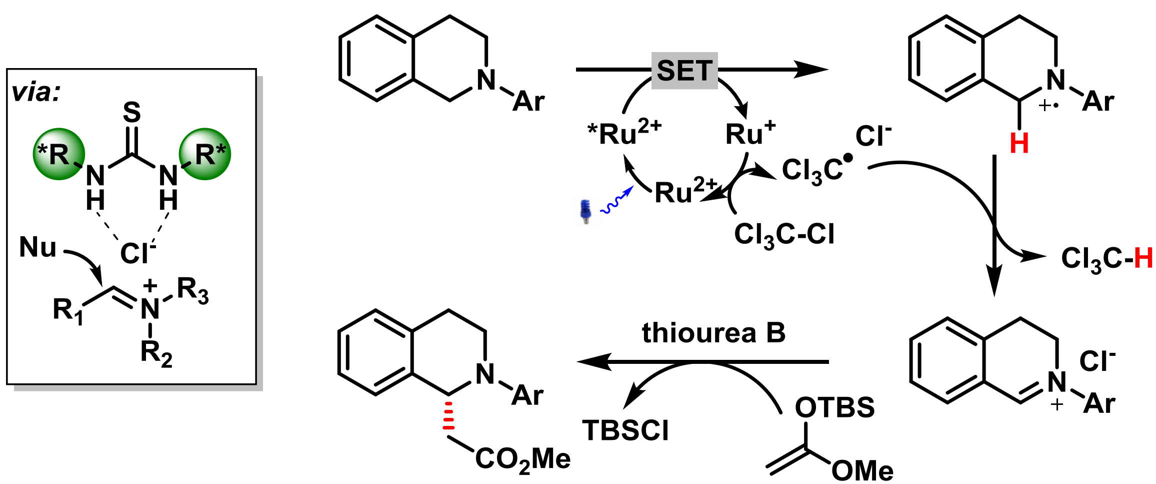
E.N. Jacobsen



up to 72% yield, 99% ee

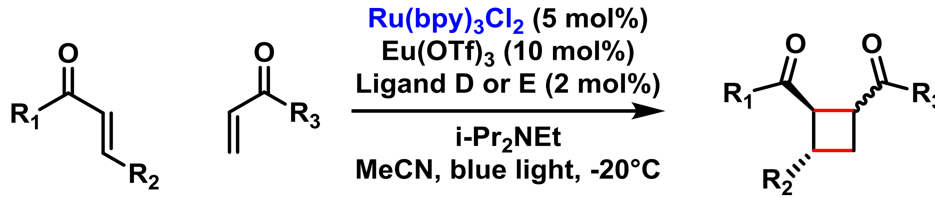


Proposed mechanism:

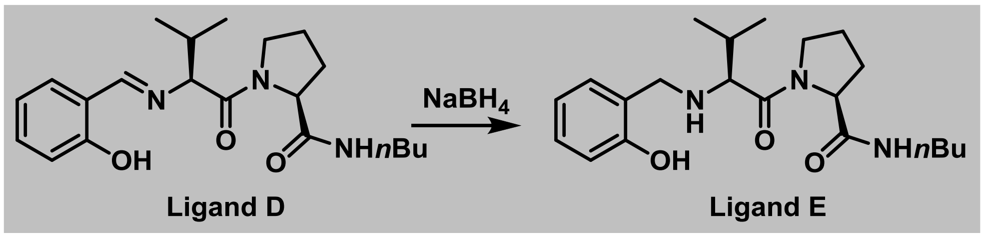


Bergonzini, G.; Schindler, C. S.; Wallentin, C.-J.; Jacobsen, E. N.; Stephenson, C. R. J. *Chem. Sci.* **2014**, *5*, 112

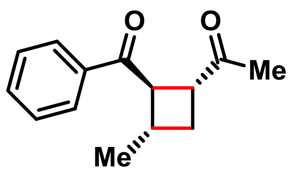
Enantioselective [2+2] Cycloaddition of Enones. Dual Lewis Acid and Photoredox Catalysis



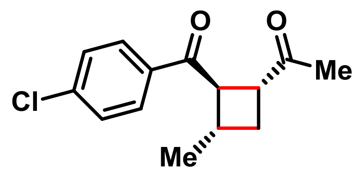
up to 80% yield
9:1 d.r., 97% ee



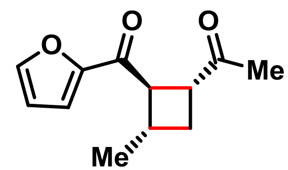
From ligand D:



71% yield
7:1 d.r., 92% ee

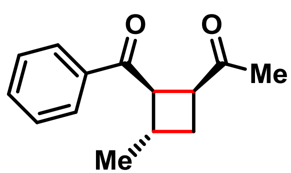


65% yield
7:1 d.r., 90% ee

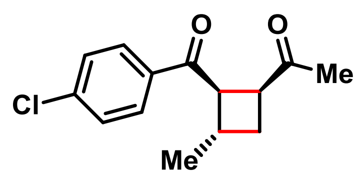


72% yield
8:1 d.r., 93% ee

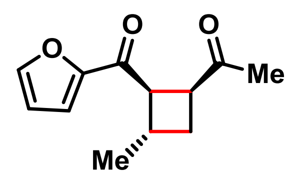
From ligand E:



78% yield
4.5:1 d.r., 95% ee



79% yield
3.5:1 d.r., 95% ee

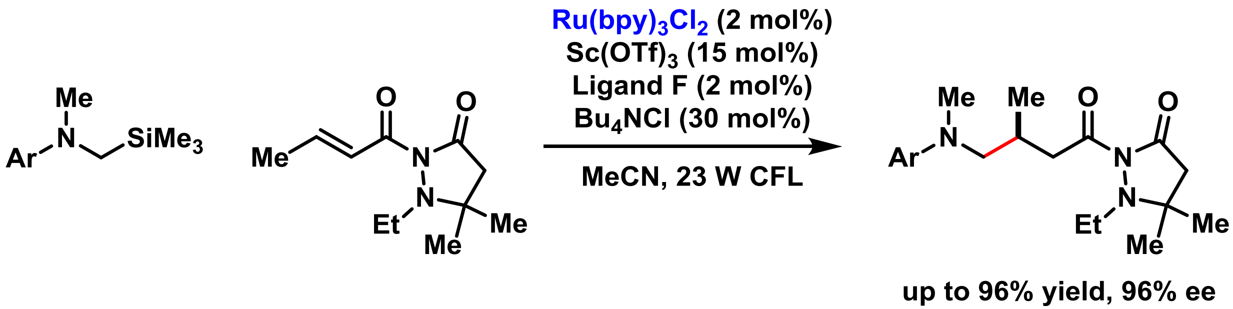


70% yield
2:1 d.r., 86% ee

Du, J.; Skubi, K. L.; Schultz, D. M.; Yoon, T. P. *Science* **2014**, *344*, 392

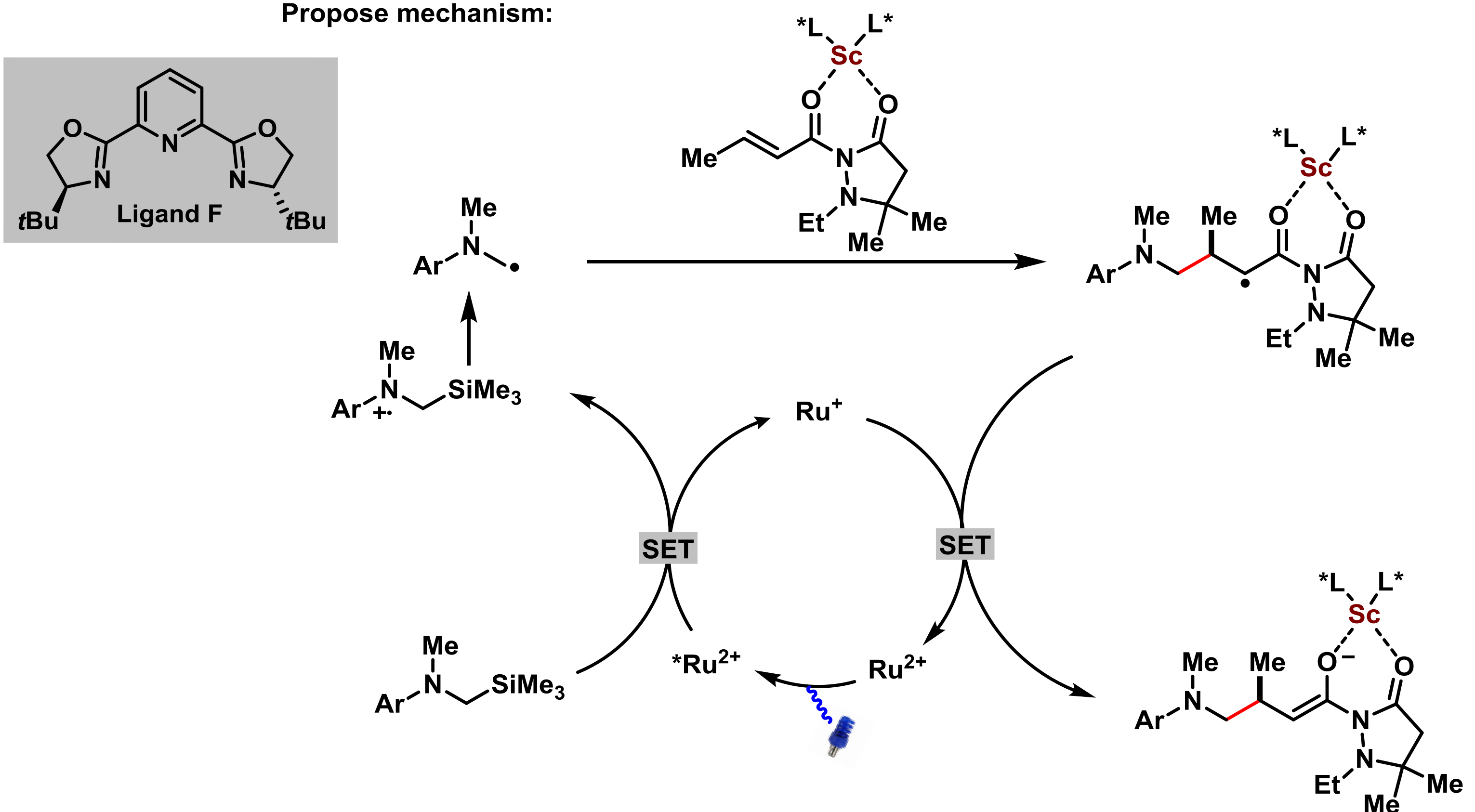
WISCONSIN
UNIVERSITY OF WISCONSIN–MADISON

Enantioselective Additions of α-Amino Radicals. Cooperative Lewis Acid and Photoredox Catalysis



T.P. Yoon

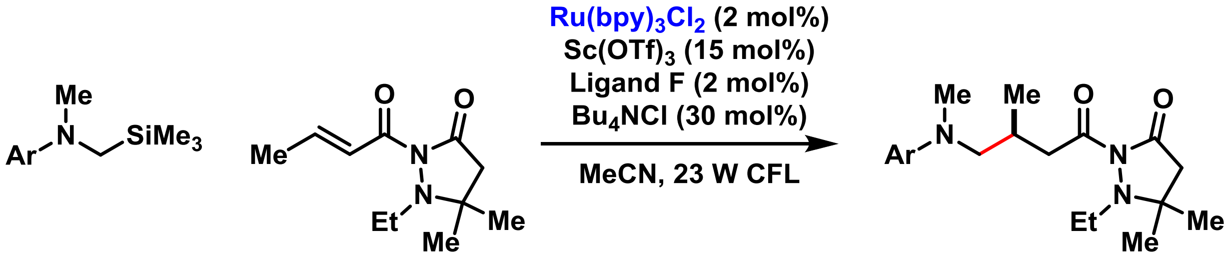
Propose mechanism:



Ruiz Espelt, L.; McPherson, I. S.; Wiensch, E. M.; Yoon, T. P. *J. Am. Chem. Soc.* **2015**, *137*, 2452.

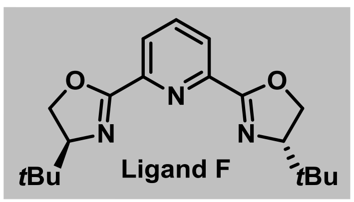
Enantioselective Additions of α-Amino Radicals. Cooperative Lewis Acid and Photoredox Catalysis

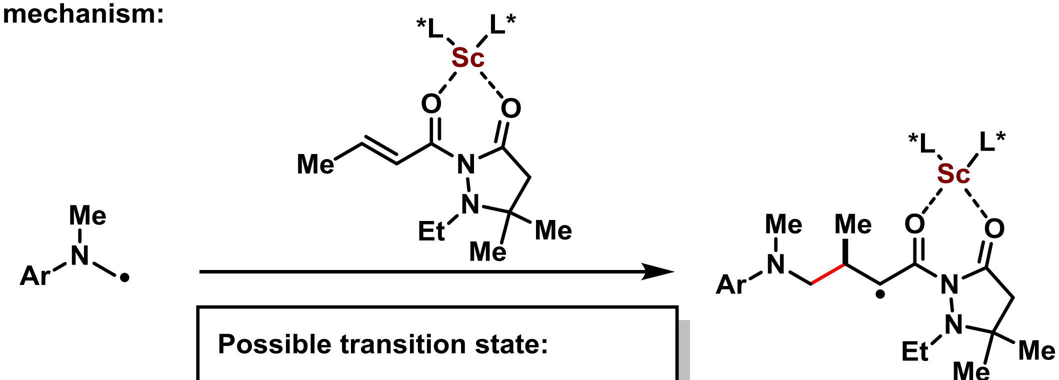
T.P. Yoon

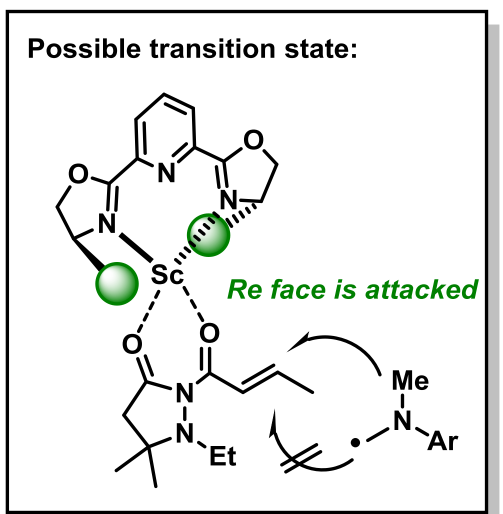


up to 96% yield, 96% ee

Propose mechanism:





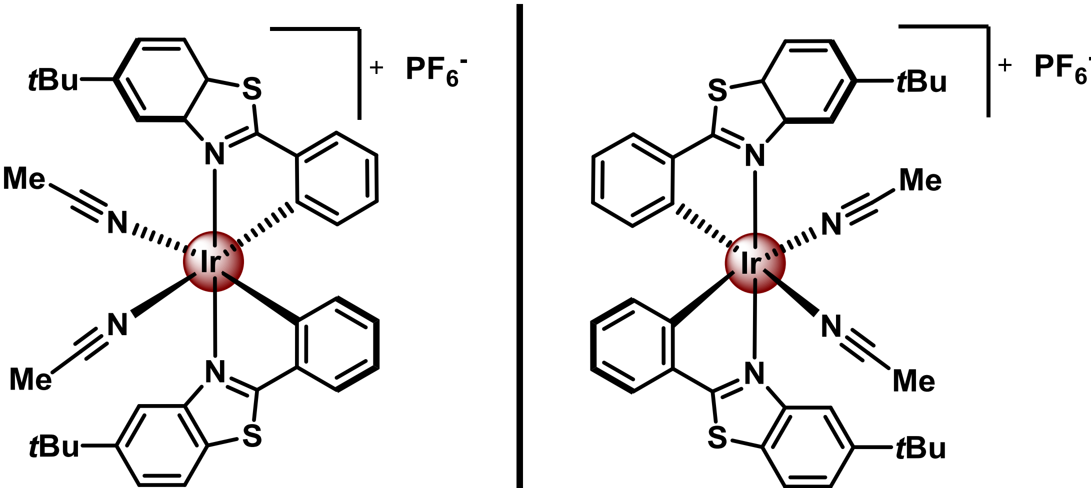


Ruiz Espelt, L.; McPherson, I. S.; Wiensch, E. M.; Yoon, T. P. *J. Am. Chem. Soc.* **2015**, *137*, 2452.

Visible Light induced Oxidation and Enantioselective Alkylation of Ketones with Chiral Iridium Catalyst

E. Meggers

Chiral Iridium Complexes for asymetric photoredox catalysis



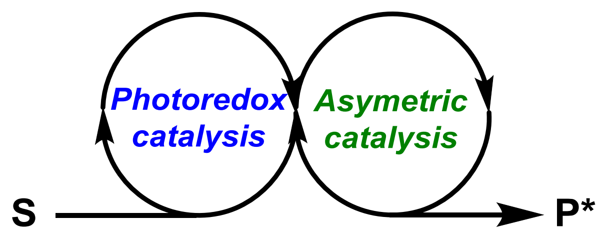
Δ-Ir G

Λ-Ir G

- Two bidentates achiral ligands in propeller-type fashion
- Two labile-exchange ligands
- Metal-centered chirality

- Chiral centre
- Catalitically active LA centre
- Photoredox centre

Two connected catalytic cycles from one catalyst

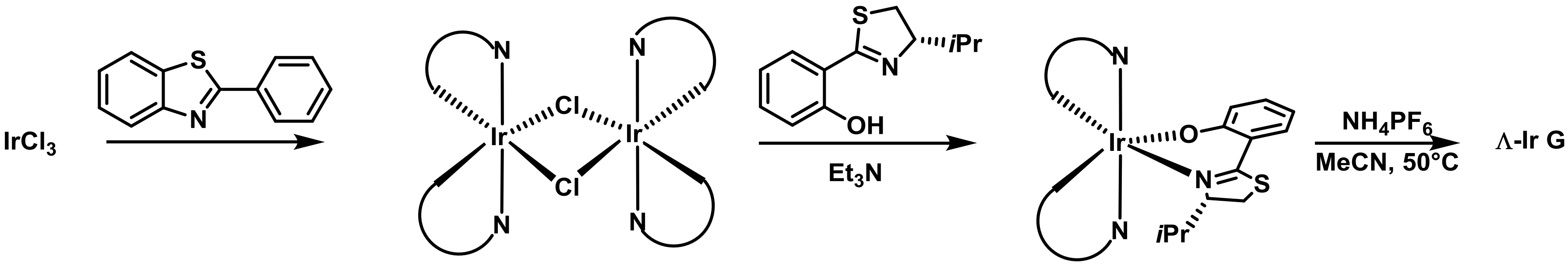


Huo, H.; Shen, X.; Wang, C.; Zhang, L.; Rose, P.; Chen, L.-A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100.

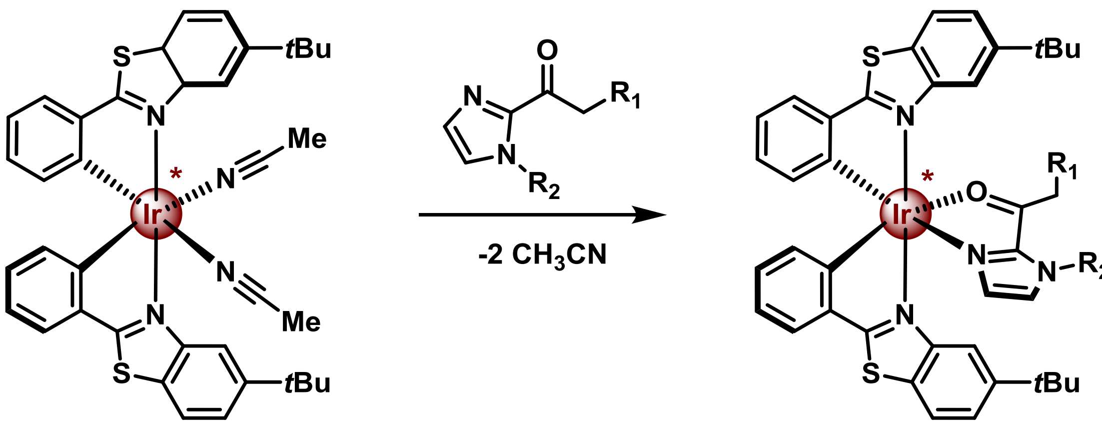
Visible Light induced Oxidation and Enantioselective Alkylation of Ketones with Chiral Iridium Catalyst

E. Meggers

Preparation of chiral Iridium Complexes



Origin of chirality: two labile acetonitrile ligands give access to a Lewis acid chiral metal centre



Huo, H.; Shen, X.; Wang, C.; Zhang, L.; Rose, P.; Chen, L.-A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100.

Visible Light induced Oxidation and Enantioselective Alkylation of Ketones with Chiral Iridium Catalyst

E. Meggers

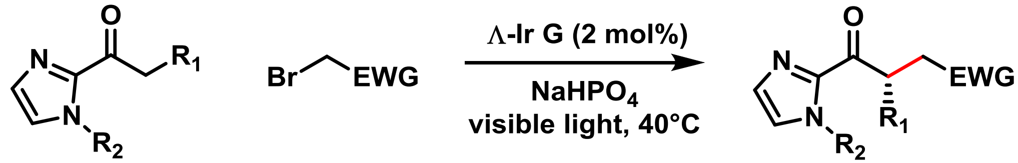
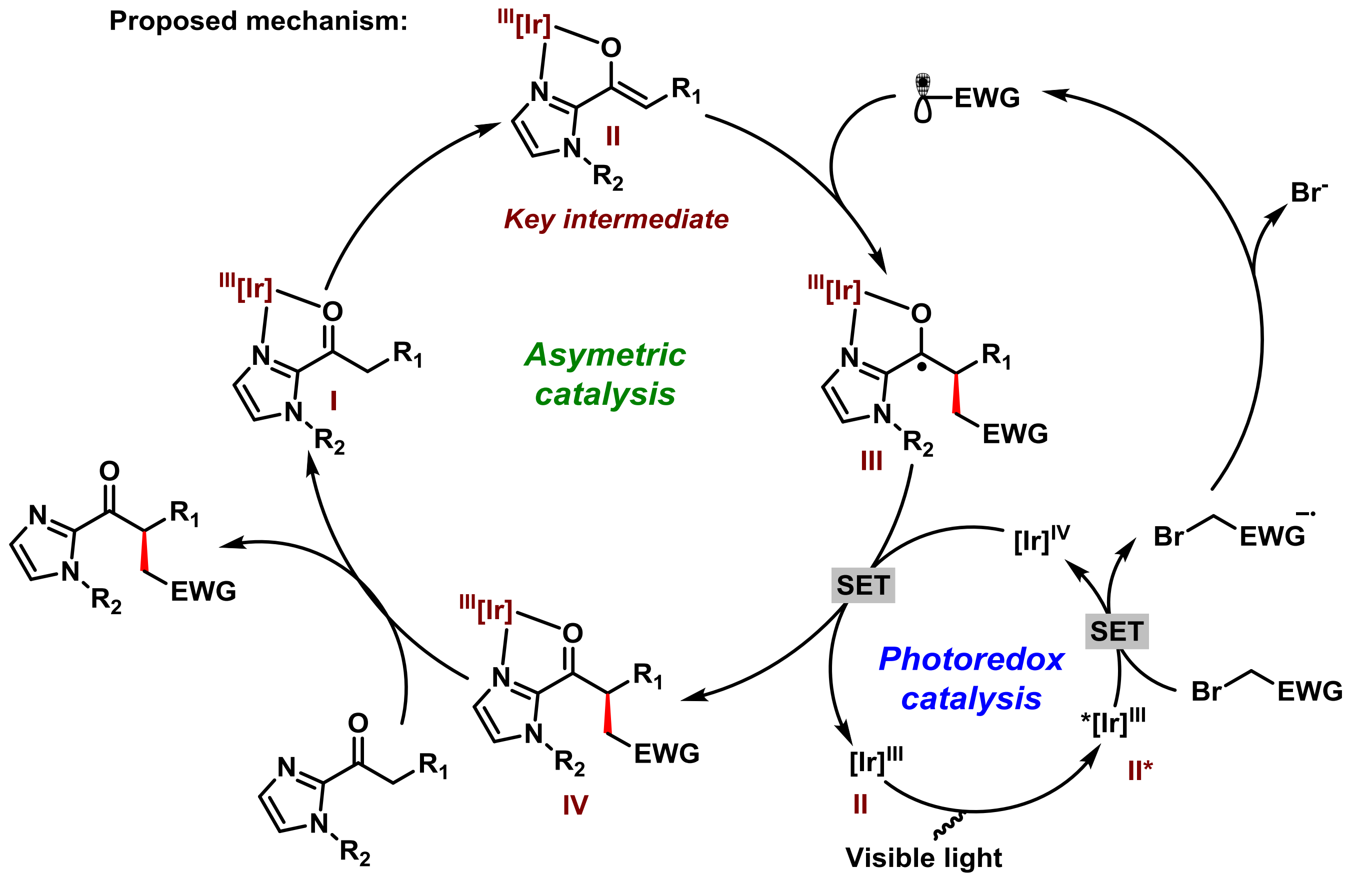


Photo-reductive activation

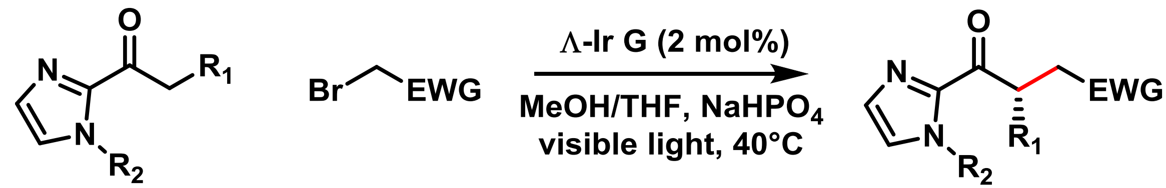
Proposed mechanism:



Huo, H.; Shen, X.; Wang, C.; Zhang, L.; Rose, P.; Chen, L.-A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100.

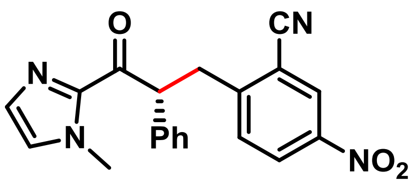
Visible Light induced Oxidation and Enantioselective Alkylation of Ketones with Chiral Iridium Catalyst

E. Meggers

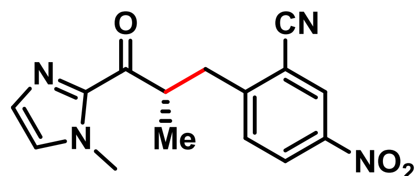


15 examples
up to 100% yield, 99% ee

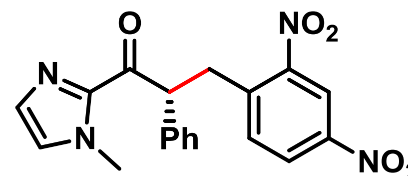
Selected examples:



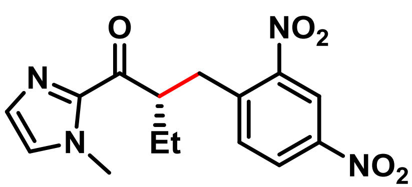
100% yield, 99% ee



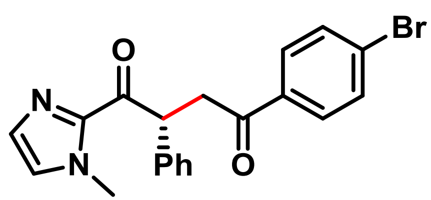
87% yield, 87% ee



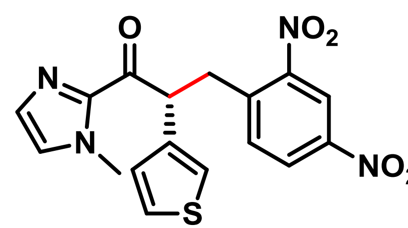
97% yield, 99% ee



84% yield, 91% ee



86% yield, 91% ee

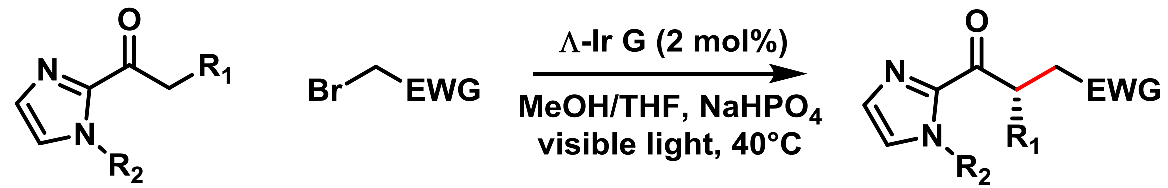


99% yield, 97% ee

Huo, H.; Shen, X.; Wang, C.; Zhang, L.; Rose, P.; Chen, L.-A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100.

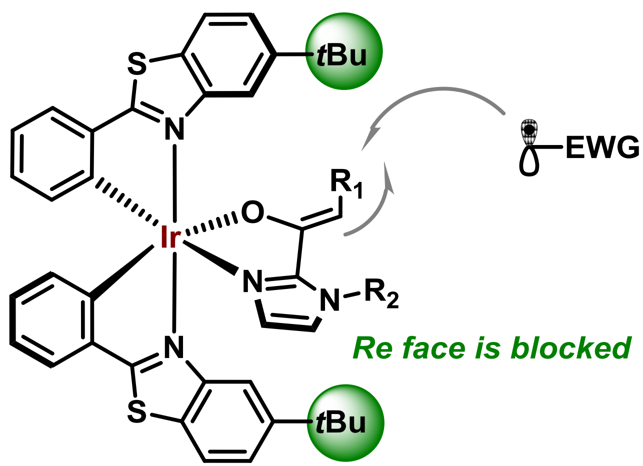
Visible Light induced Oxidation and Enantioselective Alkylation of Ketones with Chiral Iridium Catalyst

E. Meggers



15 examples
up to 100% yield, 99% ee

Model for asymetric induction: enolate complex



Huo, H.; Shen, X.; Wang, C.; Zhang, L.; Rose, P.; Chen, L.-A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100.

Visible Light induced Oxidation and Enantioselective Alkylation of Ketones with Chiral Iridium Catalyst

E. Meggers

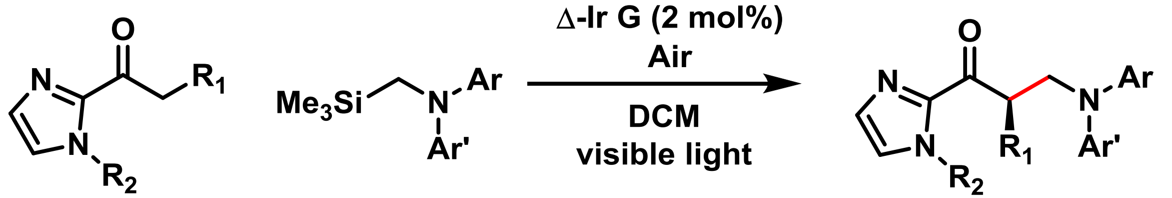
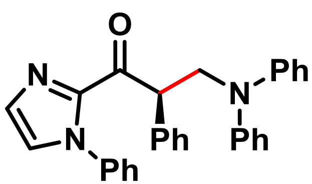


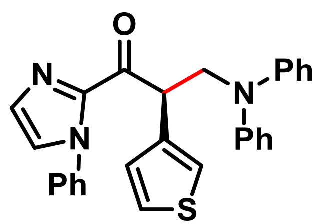
Photo-oxidative activation

12 examples
up to 96% yield, 98% ee

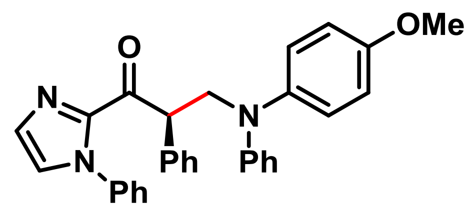
Selected examples:



92% yield, 97% ee



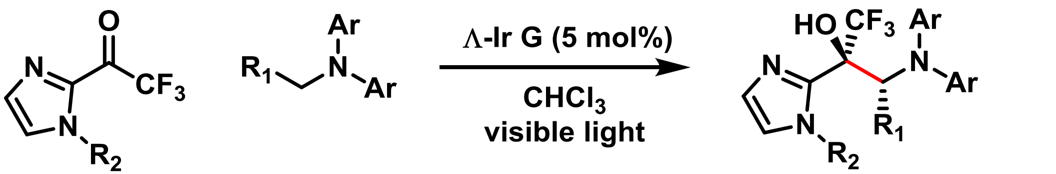
62% yield, 94% ee



90% yield, 95% ee

Huo, H.; Shen, X.; Wang, C.; Zhang, L.; Rose, P.; Chen, L.-A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100.

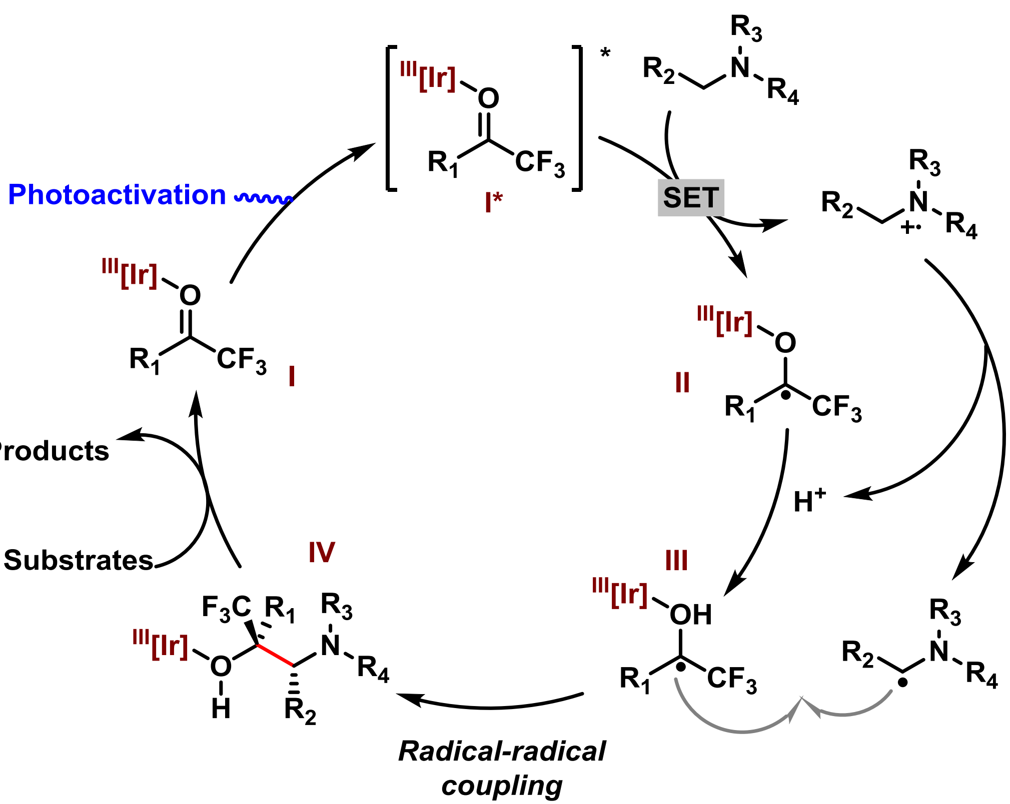
Asymetric Radical-Radical Cross-Coupling Through Visible-Light Activated Iridium Catalysis

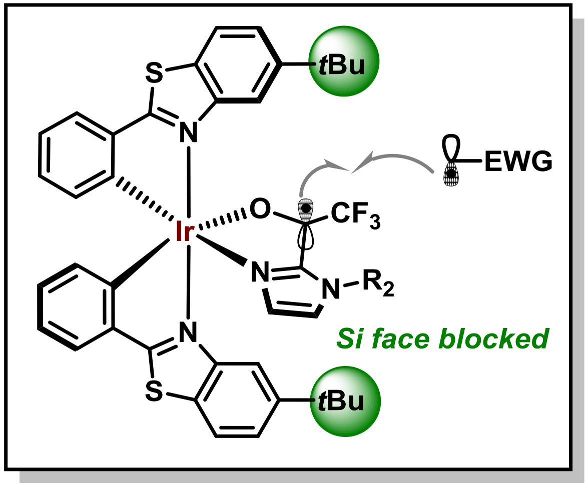


14 examples
57-97% yield, up to 99% ee

E. Meggers

Proposed mechanism for radical-radical coupling:

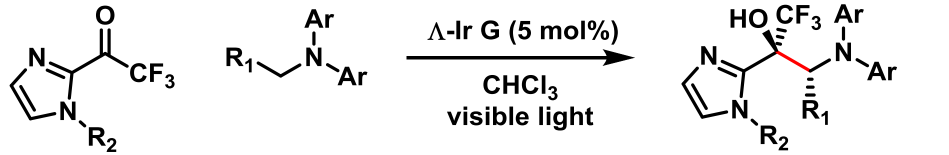




Wang, C.; Qin, J.; Shen, X.; Riedel, R.; Harms, K.; Meggers, E. *Angew. Chem. Int. Ed.* **2016**, *55*, 685.

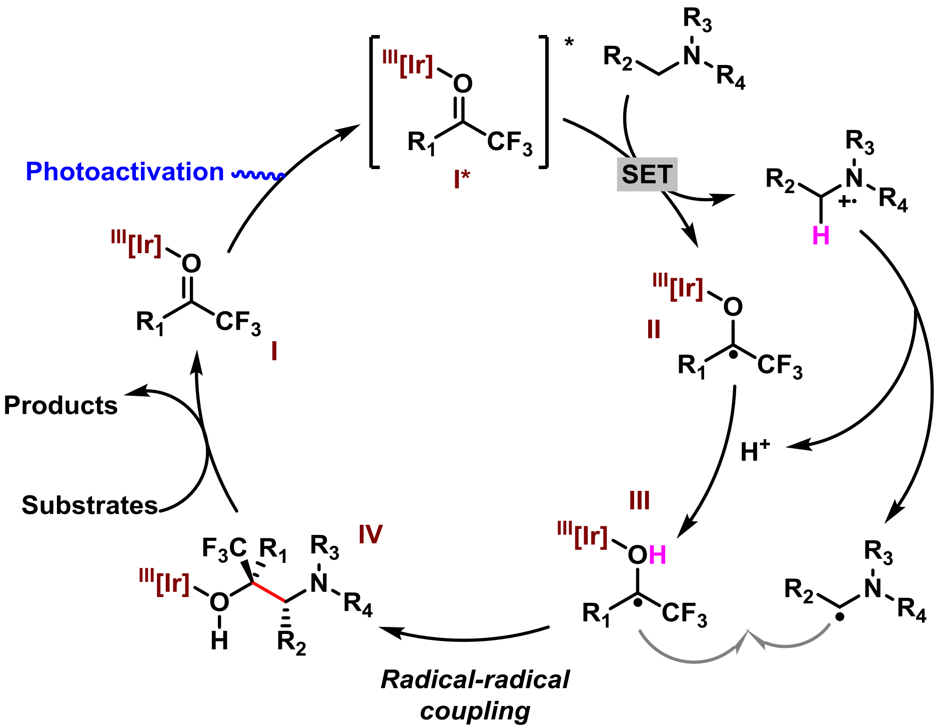
Asymetric Radical-Radical Cross-Coupling Through Visible-Light Activated Iridium Catalysis

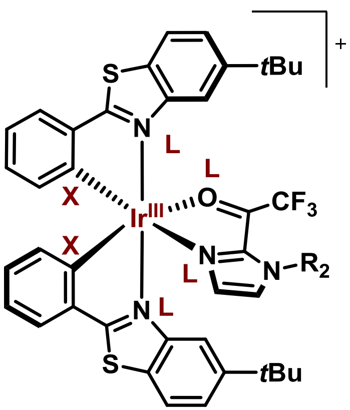
E. Meggers



14 examples
57-97% yield, up to 99% ee

Proposed mechanism for radical-radical coupling:





O.D. = 2+1 = 3

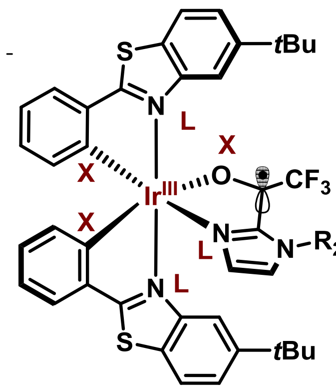
I

X= ligand give 1e-

L= ligand give 2e-

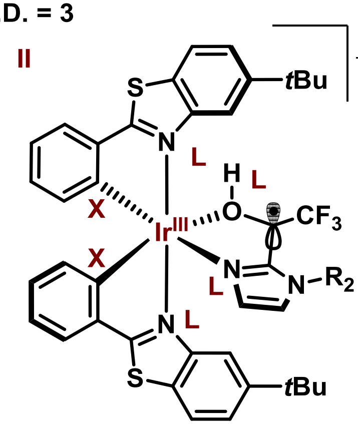
O.D.= x+q

q= global charge



O.D. = 3

II

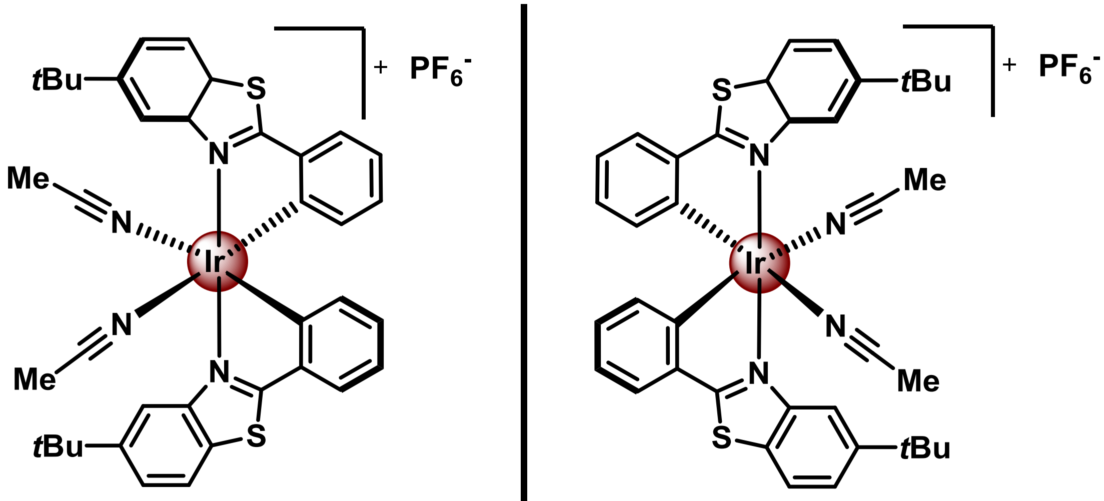


O.D. = 2+1 = 3

III

Wang, C.; Qin, J.; Shen, X.; Riedel, R.; Harms, K.; Meggers, E. *Angew. Chem. Int. Ed.* **2016**, *55*, 685.

Summary



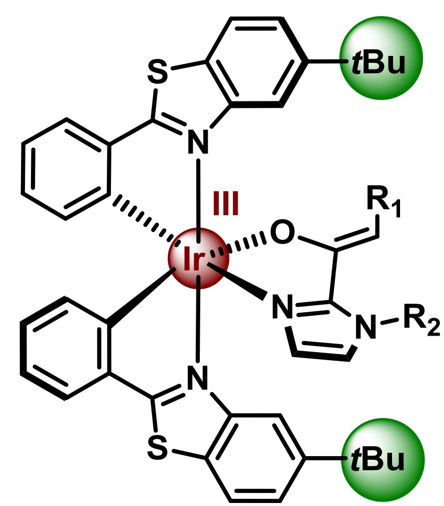
Δ-Ir G

Λ-Ir G

- Chiral centre
- Catalitically active LA centre
- Photoredox centre

Key intermediate Ir(III):

- Nucleophilic intermediate in the asymmetric catalysis
- *In situ* generated active visible-light photosensitizer

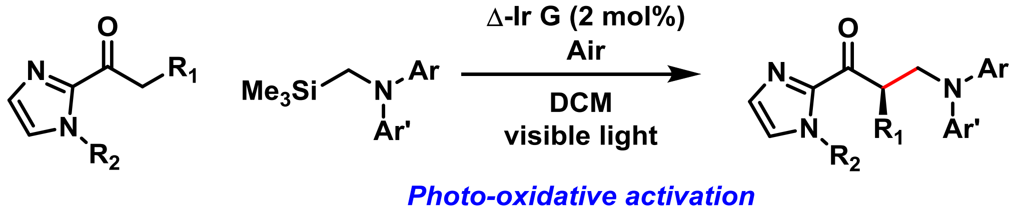


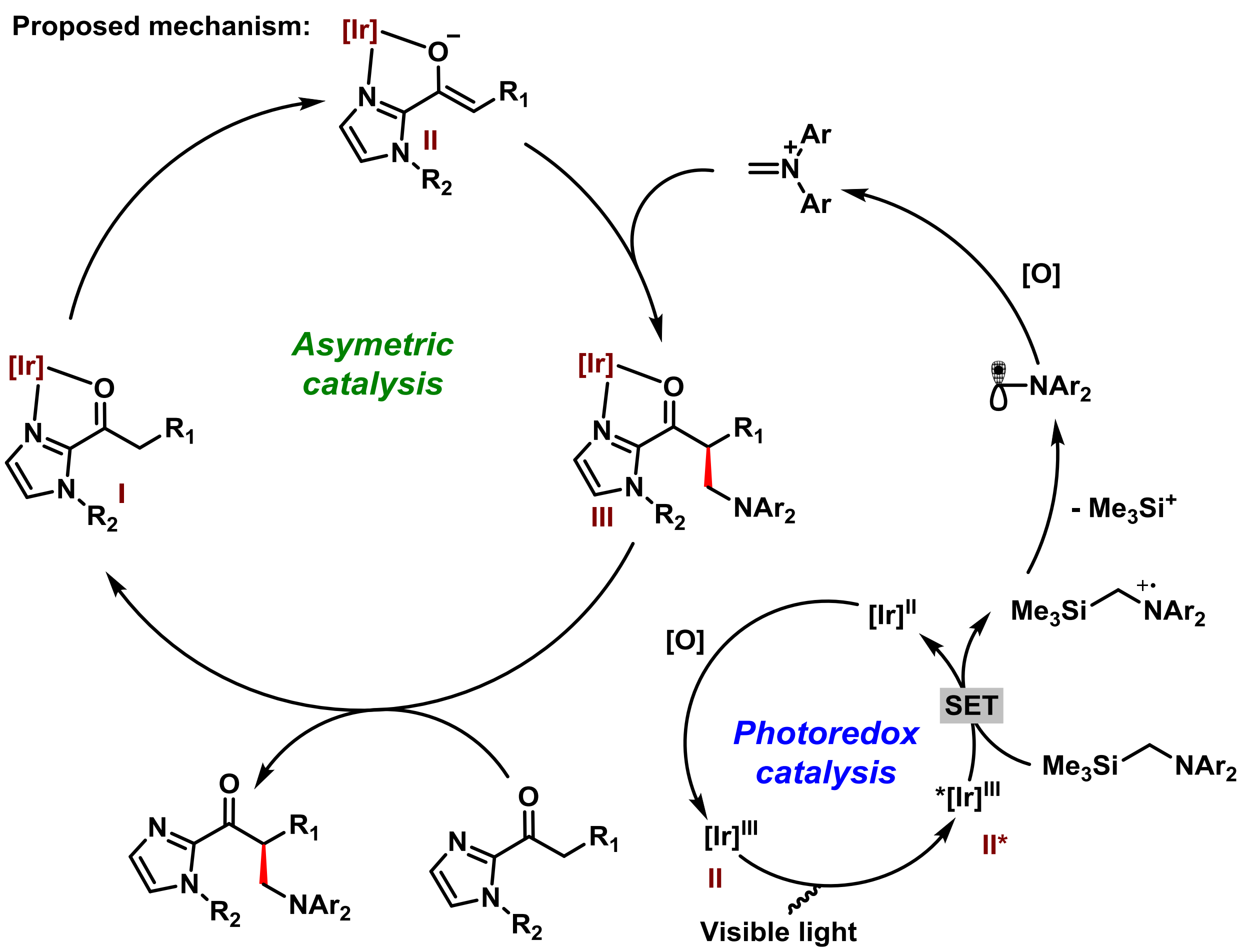
Ir(III) enolate complex

ANNEXE

Asymetric α-Aminoalkylation of Acyl Imidazoles with Chiral Iridium Catalyst

E. Meggers





Wang, C.; Zheng, Y.; Huo, H.; Röse, P.; Zhang, L.; Harms, K.; Hilt, G.; Meggers, E. *Chem. Eur. J.* **2015**, *21*, 7355